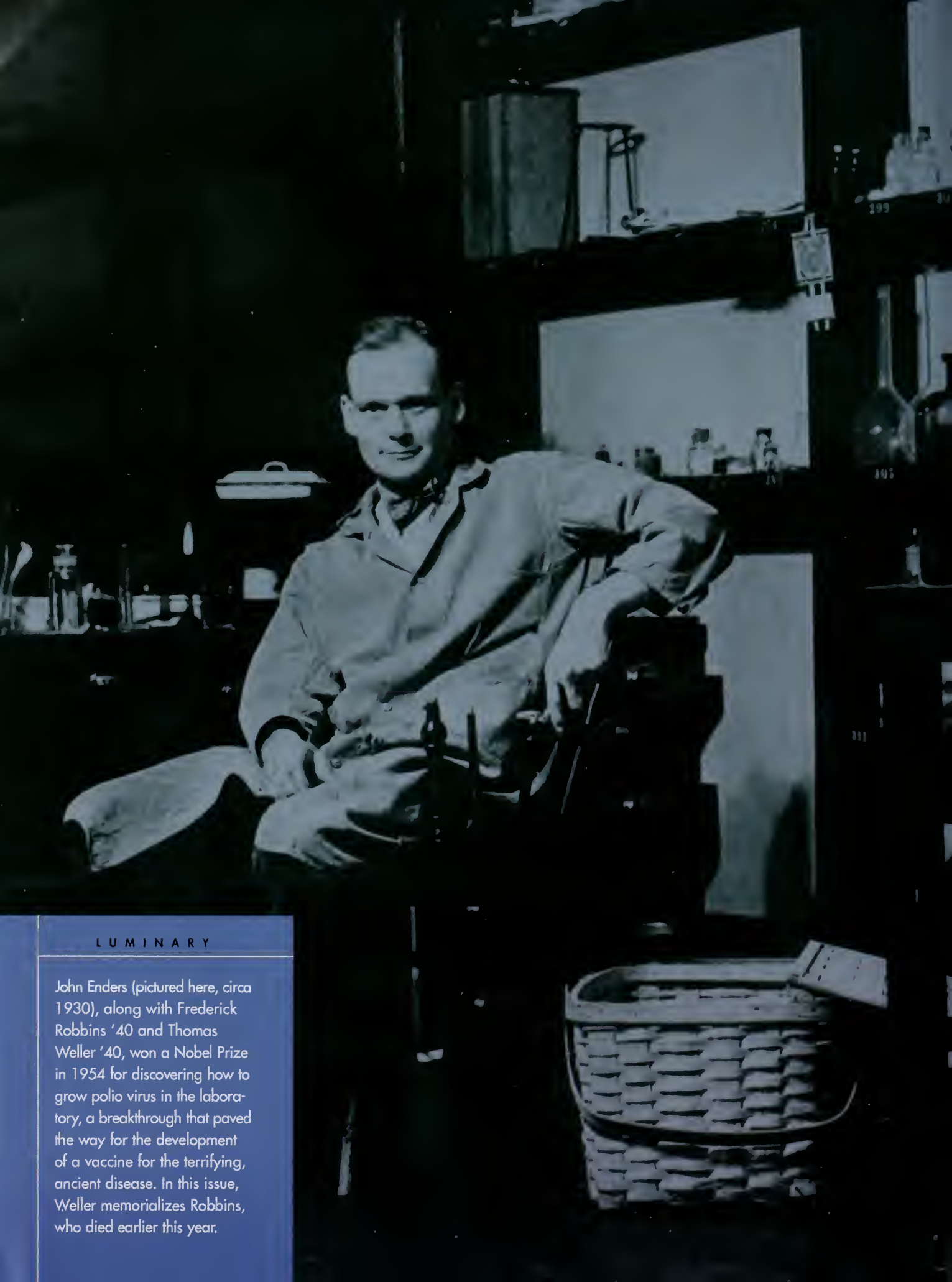
AUTUMN 2003

Harvard Medical

ALUMNI BULLETIN

CREATIVE IMPULSES

Neurobiologists illuminate our instincts for the arts



LUMINARY

John Enders (pictured here, circa 1930), along with Frederick Robbins '40 and Thomas Weller '40, won a Nobel Prize in 1954 for discovering how to grow polio virus in the laboratory, a breakthrough that paved the way for the development of a vaccine for the terrifying, ancient disease. In this issue, Weller memorializes Robbins, who died earlier this year.

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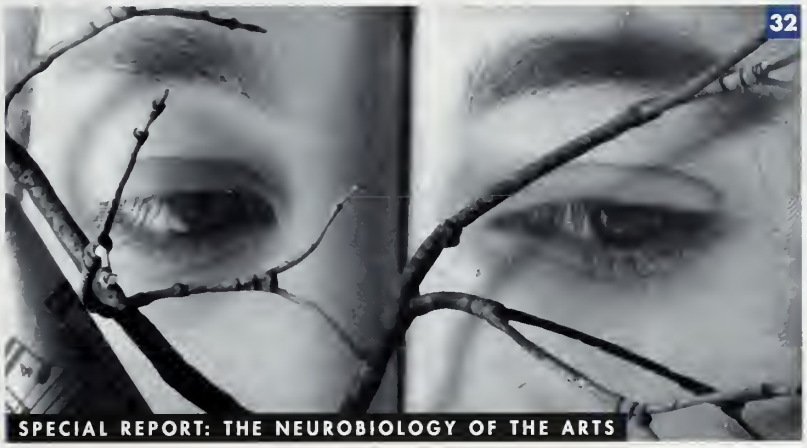
Cover image: Meditating Philosopher, *by Rembrandt van Rijn, courtesy of Réunion des Musées Nationaux. Erich Lessing, Art Resource, New York*



FEATURES

Harvard Medical
ALUMNI BULLETIN

In This Issue

LONG AGO, IN A GALAXY THAT SEEMS INCREASINGLY FAR AWAY, I SAT BY A fire and ehatted with Bette, a friend whose tastes are on the high end of literary. Thinking that I had some passing aequaintance with ehemistry, an impression my professors at HMS would have been quiek to refute, she asked a little sadly whether it spoiled the fire for me to know what was happening in it, whether information turned the mystery into materialism. The question astonished me then, and it does now. Even granting that fires are too eomplex really to eomprehend, the little I knew about vaporization and oxidation hardly detracted from the beauty of the moment and eertainly did not diminish my sense of wonder, whieh is what I think she feared from the ineursion of seienee into aestheties.

A eommon romantie heresy is that information makes us jaded; it is sometimes expressed as the fear that ehildren will lose their sense of wonder if they are edueated. But it seems to me that ehildren don't eome equipped with an innate sense of wonder. They take experienee at faee value and rarely bother to ask why things are as they are, and not some other way. (Toddlers' ineessant "why" questions are really an effort to figure out what kind of answer they will get when they use the word "why" and are in the same vein as questions about how to work the remote eontrol.) The sense of wonder, as opposed to operational euriosity, is generally an adult prerogative, for it takes a lot of knowledge to be felt at all deeply.

I think my old friend might be not merely saddened but appalled by this issue of the *Bulletin*, whieh explores the neurobiology underlying some aspeets of painting, literature, and musie. It is one thing to think that knowing the chemistry of cadmium yellow or the physies of a string under tension will make an aesthetie experienee—the painted image of an urban sunset, the sound of eight eellos and a soprano—less transeendent. That's bad enough. But when you turn to the brain, as some of the neurobiologists featured in this issue do, and find that the sublime appreeiation for a Baeh fugue or Monet's brush-stroked poppies appears to be an outgrowth of basie primate wiring diagrams—eireuitry that seems to be about aequiring meat with the eooperation of one's nearest and dearest, or about not becoming meat to a stranger—I can hear Bette say, "Spare me the details." I don't agree, but, then again, I never did.

William Ira Bennett

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> "It is hard to imagine anything more expensive to medical care budgets—and more profitable to pharmaceutical companies—than interminable treatment with drugs that don't work."
>
> —KARL E. HUMISTON '55, KEIZER, OREGON

Sacrificial Rites

Congratulations on the fine special report on money and medicine, "Don't Fence Me In," in the Spring 2003 issue of the *Bulletin*. Medical care has indeed become an intrinsically valuable commodity, and I would like to offer an additional perspective on this.

During the first seven years of my life, my grandfather, as a member and chairman of the American Medical Association's Council on Medical Education, labored mightily to strengthen the role of scientific research in medical training and practice. The fundamental rituals of science helped elevate physicians, who became the only health professionals with the legal authority to prescribe the therapeutic drugs produced by this science. My grandpa's efforts were successful. Today's highly developed procedures—such as FDA approval, medical training, and standards of practice and licensing—are inseparable from their roots in scientific ritual.

Today's approved treatments are those that have been proven to help most people with a particular pathology, typically about two-thirds. The fact that the same research has typically shown that a third of patients tend to fail to benefit seems to have slipped through the cracks. Today's rather inflexible rituals of practice require prescribing only those treatments that have been scientifically proven to help most people, whether they help a specific patient or not. Perhaps not in academic settings, where such things are more closely scrutinized, but assuredly in general throughout the nation, this is so.

It is hard to imagine anything more expensive to medical care budgets—and more profitable to pharmaceutical companies—than interminable treatment with drugs that don't work. Our rituals are no longer serving their original purpose of ensuring purity of practice. I do not see how either financial reform or tighter regulation of practice can have much benefit without changing the ritual (which is, admittedly, extraordinarily difficult to do). The beneficial change that I envision is simply to bring about the inclusion, in the policy and standards of practice books, both procedures for identifying those individuals not being helped by the standard approved treatments and procedures for selecting alternative treatments for them.

Many physicians would love to do just that, but have been restrained by the absence of necessary policies, procedures, and standards of practice authorizing them to do so without jeopardizing their pay and position.

In mid-career, I became aware that, as a graduate of HMS, I was looked upon with some suspicion as having come from a school where students learned to think for themselves and to apply scientific principles in their true sense, not just follow established protocol for its own sake. I am grateful that this appears to be so.

KARL E. HUMISTON '55
KEIZER, OREGON

Dollars and Sense

In "A Fistful of Dollars," in the spring issue of the *Bulletin*, the panel, incredibly, failed to notice the elephant in the living room. The pre-eminent cause of our health care system's malaise—not addressed by the panel—is private insurers' pursuit of corporate profit. This is a prime reason why half of the $1.6 trillion a year we spend on health care goes to health care business, not health care benefits. This is the reason that up to 25 percent of private insurers' premium income goes to advertising, administration, mega executive salaries, and profit, while Medicare's overhead is under 3 percent. This is the reason we spend two to three times as much on health care per capita as any other industrialized country and yet we, alone, have 43 million mostly working citizens with no health insurance. This is why Americans covered by private, employer-based insurance are restricted in their free choice of doctor and hospital and why their doctors' autonomy has been decimated. This is the reason the World Health Organization ranked our inefficient, absurd, and cruel

system 37th in the world in 2000. In the category of "fairness," we ranked 54th.

While the panel did not see the elephant, they did see the solution as more complex than it needs to be. Once we stop treating health care as a free-market commodity and treat it as a societal obligation, our solution would be the same one accepted by all other developed countries in their various, generally popular, government-run systems. And we would save money, too. An improved Medicare for all would save billions by spreading the risk to the young and healthy, not just the old and sick. Further huge savings—hundreds of billions, says the Congressional Budget Office—would be realized by eliminating advertising, marketing, and profit and by vastly simplifying administration.

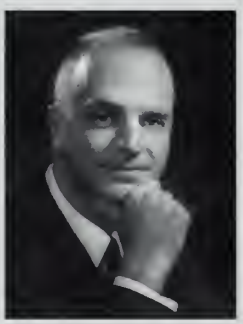
The panel worried about the prospect of long waits for non-emergency care as in some other nations. But, as noted, other countries spend far less on health care than we do. Dr. Marcia Angell stated it well in a *New York Times* op-ed piece in October 2002: "If they were to put the same amount of money as we do into their systems, there would be no waits. For them, the problem is not the system; it's the money. For us, it's not the money; it's the system."

Since organized medicine was represented on the panel, a more rounded discussion would have occurred had you included a leader of the national Physicians for a National Health Program, several of whom are in the HMS community.

JAMES S. BERNSTEIN '52
ROCKVILLE CENTRE, NEW YORK

RACE TO THE FINISH

I would like to express my deep appreciation to Farrokh Saidi '54 for his kind words about my father, Robert "Hawk" Shaw '45, in Dr. Saidi's account about the gripping challenges he has faced since his return to Iran to practice medicine (Spring 2003 issue). Dad always spoke of Dr. Saidi with the strongest admiration and affection.



Robert "Hawk" Shaw

I also wanted to mention that in editing Dad's obituary for publication in that same spring issue, the *Bulletin* got the story slightly wrong—Hawk's first wife, Laura ("Cricket"), did not survive him. She died in August 1998, which prompts me to launch, Dad-like, into a possibly true story about two of our founding fathers. Thomas Jefferson and John Adams were fast friends in their revolutionary youth, but in 1800 they had a grave falling out after the bitterly contested presidential election ended with Adams stepping down as U.S. president after one term, and Jefferson taking his place. The ice thawed between them about 12 years later.

But old competitions die hard. One version of the story says that, in their final years, each of these last two surviving founding fathers vowed he would outlive the other. In fact, both died on Independence Day 1826, Jefferson just a few hours before Adams. But Adams didn't get the news in time to savor his short victory. His last words are said to have been, "Thomas Jefferson survives!"

This story is particularly appealing to Hawk and Cricket's children, who suspect those two also had an unspoken competition to outlast the other. Dad won the competition hands down, but it appears fate gave Mom a paper victory this spring in the *Bulletin*.

LIBBY SHAW
WATERTOWN, MASSACHUSETTS

Mass Appeal

I wanted to compliment you on the excellent spring issue. I can't tell you how much I look forward to receiving the *Bulletin* with its fine articles and the news about my friends at Massachusetts General Hospital in the '40s, '50s, and '60s. I was saddened to read about the tragic deaths of Dr. and Mrs. Arthur Guyton '43A after the wonderful write-up about them that appeared in just the previous issue. Thank you, again, for doing such a great job.

WINFIELD S. MORGAN, MD
PURSGLOVE, WEST VIRGINIA

The Bald Truth

I enjoyed reading "Heavy Metal," Donald Bickley's interesting collection of stories in the Spring 2003 issue of the *Bulletin*. As a dermatologist, I was particularly intrigued by the thallium story, in which Dr. Bickley describes a group of young women who permanently lost their scalp, eyebrow, and eyelash hairs, presumably as a result of using a depilatory cream containing thallium acetate.

That story prompted me to remember that during my dermatology residency, I had read that thallium was at one time used therapeutically to cause depilation in patients with tinea capitis. Several of my old textbooks confirm that history. In addition, both Moschella's *Dermatology* (1975) and Rook's *Textbook of Dermatology*, Third Edition (1979), state that the hair loss due to thallium is reversible, unlike the situation with Dr. Bickley's patients. Perhaps his patients' hair loss was not caused by the direct toxic effects of the thallium in the cream they used.

MASSAD GREGORY JOSEPH '77
SOUTH PASADENA, CALIFORNIA

The Bulletin welcomes letters to the editor. Please send letters by mail (Harvard Medical Alumni Bulletin, *25 Shattuck Street, Boston, Massachusetts 02115*); *fax (617-384-8901); or email (bulletin@hms.harvard.edu). Letters may be edited for length or clarity.*

A Towering Investment in Science

WITH A LONE RED CRANE TILTING in the distance—and providing the only visible reminder of almost three years of traffic-stopping construction—Harvard Medical School's new research building at 77 Avenue Louis Pasteur was officially unveiled on September 24. The speed with which the massive endeavor was carried out, and the elegance of its final product, call to mind another famously efficient project—the mapping of the human genome.

It was the human genome project, in fact, that had inspired HMS dean Joseph Martin and a quorum of colleagues to propose the new building in the first place. "We wanted to take advantage of a unique moment in the life sciences," Martin said. With the human genetic map in hand, researchers around the world have been racing to find genetic causes and cures for a variety of human illnesses. To jump start that quest, Martin and his colleagues had the idea to gather researchers from the clinical and basic science worlds, including the Departments of Pathology and Genetics, under one roof.

The architects clearly took the theme of collaboration to *(continued on page 6)*

ON COMMON GROUND: The new research building will invite researchers and clinicians to collaborate in the search for genetic causes and cures.

THE CLASS OF 2007

The newest members of the HMS community—the Closs of 2007—donned their white coots in August. The closs is 51 percent women ond 49 percent men. Twenty-one percent of the students ore Asion Americons, 16 percent Africon Americons, 10 percent Lotinos, ond 2 percent Notive Americons. The closs includes representotives of 33 stotes, plus the District of Columbio, ond 12 foreign countries: Brozil, Conodo, the Dominicon Republic, Germony, Greece, Hoiti, Indio, Jomoico, Kenyo, Mexico, Nigerio, ond Toiwon. Ten members of the closs ore MD/PhD students.

The youngest entering medicol student is 21 yeors old, the oldest is 32, ond the medion oge is 23. Roughly two-thirds of the closs mojored in the sciences while undergroduotes; 10 percent mojored in the sociol sciences, 10 percent in the humonities, ond 13 percent in other mojors ond/or double mojors. ■

RITE STUFF: After receiving his white coat, Matthew McCarthy '07 is congratulated by Augustus White, Holmes Society master.

YIELD OF DREAMS: The new building

(*continued from page 5*)

heart. From its revealing glass façade, which draws in even the casual passerby, to its expansive, open-plan laboratories and wood-paneled hallways, dotted with nooks, plazas, and gardens, the building seems to be one big invitation to come explore. The half-million-square-foot structure, with a price tag of $260 million, includes a ten-story tower looming above a four-story wing facing Avenue Louis Pasteur.

"We sought to make the building a part of, not a satellite of, Harvard Medical School and its teaching hospitals," Martin said. "Many researchers and clinicians will join hands and forces here to work on the mission of alleviating human suffering caused by disease."

Lawrence Summers, president of Harvard University, expressed pride in the new endeavor and high hopes for its mission. "As a consequence of what happens in this building," he said at the ribbon-cutting ceremony, "many, many people at this university, in this city, in this country, and in the world will be far better off." ■

Misia Landau is the senior science writer for Focus.

A Systematic Approach

HARVARD MEDICAL SCHOOL HAS announced the creation of the Department of Systems Biology (DSB), one of the first department-level systems biology programs in the nation. Systems biology seeks to build from current knowledge of genetic and molecular function to an understanding of how a whole cell works as a system, and from there to an understanding of multicellular systems.

The DSB will be the first completely new department at HMS in more than 20 years and, with more than 20 faculty recruitments expected, will be one of the School's largest. The first chair of the new department, Marc Kirschner, is a pioneering cell biologist who led the 1993 formation of the School's Department of Cell Biology and in 1999 helped create the Harvard Institute for Chemistry and Cell Biology.

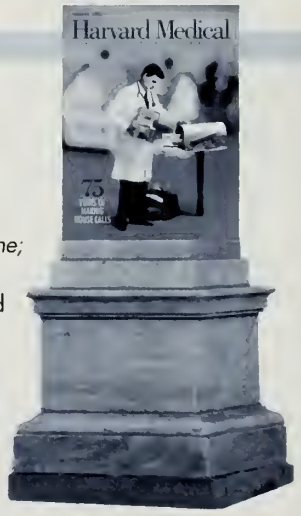
"As we understand more about the tiniest pieces that we are made of, it becomes increasingly clear that we do not understand how they work together as systems," Kirschner says. "We need to build on the foundation of molecular biology to construct an understanding of the architecture of the cell and how cells cooperate across organ systems, with a predictive model of physiology as the ultimate goal."

Two other founding faculty members have been named: Timothy Mitchison, the Hasib Sabbagh Professor of Systems Biology at HMS, and Lewis Cantley, HMS professor of medicine at Beth Israel Deaconess Medical Center. The department will consist of newly recruited faculty from such areas as mathematics, computer sciences, physics, and engineering, as well as from traditional biomedical fields.

The department will focus on education and will provide a learning environment to facilitate training the systems biologists of the future. "We hope this will become a model for other departments in medical schools and colleges across the country," says Joseph Martin, dean of HMS. "Biologists will need broad training in quantitative science, and physical scientists need to be exposed to new approaches to biology that make use of their talents and experience." ■

ALL IN GOOD TIME

The 75th anniversary issue of the *Bulletin* recently received several national honors: a gold medal Eddie Award from *Folio: Magazine;* a Clarion Award from the Association for Women in Communications; and an Award of Distinction from the Association of American Medical Colleges. The most enduring honor for the *Bulletin,* though, was having the 75th anniversary issue included in the time capsule created as part of the dedication of the New Research Building. ■



Dean Joseph Martin

The State of the School

In his annual State of the School address in October, Dean Joseph Martin recapped "an extraordinary year" at HMS that saw the opening of the largest building ever constructed by Harvard University and the creation of the School's first totally new basic science department in 20 years.

The events marking the dedication of the new research building "were really momentous for many of us," Martin said. "We have come to think about the structure of Harvard Medical School as two Quads separated—but only slightly—by Longwood Avenue."

Turning to the new Department of Systems Biology, Martin pointed out that "our investment in the formation of a new structure to house systems biology is a major departure from what has been done in most other institutions, where interdisciplinary or interdepartmental efforts have been made."

Martin said that creating a department for systems biology—sometimes called "the new physiology"—in some ways represents a throwback to an earlier scientific era, with its renewed emphasis on organ systems and organisms as opposed to isolated genes and proteins. Pulling up a photo of the great HMS physiologist Walter Bradford Cannon, Class of 1900, Martin recalled that "when Marc Kirschner presented some of his ideas about this back in the winter, he referred to Walter Cannon, who, I think, probably turned over in his grave when we disposed of physiology ten years ago....I think he would be pleased that we've returned to this as a focus of our efforts."

Martin also welcomed Malcolm Cox '70, who arrived in May to become dean for medical education, and Jeffrey Newton, who joined the School as dean for resource development in August. Martin recognized several HMS leaders who have assumed new responsibilities in the recent administrative reorganization: Nancy Andrews '84, as associate dean for basic science and graduate studies; Raphael Dolin '67, as dean for academic and clinical programs; and Jules Dienstag, as associate dean for academic and clinical programs. Martin led a round of applause for Dennis Kasper, who stepped down after six years as executive dean for academic programs to focus on leading the Channing Laboratory and the new biodefense and emerging infectious diseases initiative.

Exemplifying the success of collaboration in the HMS community, Martin noted, is a $24-million grant from the Donald W. Reynolds Foundation, establishing a cardiovascular clinical research center to develop new risk measures and biomarkers in atherosclerotic heart disease. The center will involve researchers from Brigham and Women's Hospital, Massachusetts General Hospital, Beth Israel Deaconess Medical Center, and HMS.

"We're very proud of that joint effort," Martin said. "It is not just a wonderful opportunity with a large amount of money, but it's an example of how collaboration can lead to a good endpoint."

Turning to education, Martin outlined recommendations of the curriculum reform task force and discussed the next steps in the multiyear process of revamping the School's medical education system. In addition to possible changes in the curriculum itself, one recommendation—spurred in part by a National Academy of Sciences report—is to review and possibly revise admission requirements to ensure that incoming students are well prepared.

"One concern expressed in the report is that too often, the definition of what college science should be is focused around passing the MCAT to get into medical school," Martin said, "and this betrays what should be a broader interest in science at the college level." ■

"Too often, the definition of what college science should be is focused around passing the MCAT to get into medical school."

A NEW LINE OF DEFENSE

HMS will establish the New England Center an Biadefense and Emerging Infectiaus Diseases (CBEID) as part af a strategic plan develaped by the Natianal Institutes of Health in the wake af the terrarist attacks and anthrax release in 2001. The CBEID will be ane af eight regional centers that will develap interventians against microbes that can be used as biaweapans, as well as emerging infectians such as West Nile and SARS.

The CBEID will suppart nine pragrams facusing an basic research and develapment of vaccines and therapeutics far the prevention and treatment af these diseases. Five af the pragrams will be based at HMS; the remaining faur will be based at Bastan University, the Center far Blaad Research in Bastan, the University af Massachusetts–Dartmauth, and the University of Massachusetts Medical Schaal.

Dennis Kasper, the William Ellery Channing Prafessar af Medicine at HMS, will serve as scientific directar af the center. ■

Dennis Kasper

Jim Yong Kim

Nawal Nour

Catchers in the Rye

AMONG THE 24 RECIPIENTS OF THE MacArthur "genius" grants for 2003, recently announced by the John D. and Catherine T. MacArthur Foundation, were two HMS alumni, Jim Yong Kim '86 and Nawal Nour '94. Each will receive a five-year, $500,000 award, with no strings attached.

"Both Jim Kim and Nawal Nour have incredible track records for developing innovative programs for helping people who have generally slipped through the significant gaps in society's safety nets," says Joseph Martin, dean of HMS. "The HMS community has been quite proud of what Jim and Nawal have already accomplished and looks forward to what they can do with the assistance of the MacArthur Foundation."

An HMS associate professor of social medicine and also of medicine at Brigham and Women's Hospital, Kim is on leave this year to work as a public health physician at the World Health Organization in Geneva, specializing in the control and eradication of infectious diseases. He has formulated new models for containing multidrug resistant tuberculosis, a disease that was once considered untreatable in many poor regions around the world. Kim has envisioned and applied effective interventions at both local and global levels and is currently mapping new strategies for international health leadership in tuberculosis, AIDS, and other infectious diseases.

Nour, who grew up in Egypt and the Sudan, is an HMS instructor in obstetrics, gynecology, and reproductive biology and the founding director of the African Women's Health Practice at Brigham and Women's Hospital. The only clinic of its kind in the United States, this practice addresses the medical and emotional needs of female immigrants who have been circumcised in their homeland. She has developed techniques for the surgical reversal of infibulation, the most severe form of the practice. By applying her skills in medicine and public health to contemporary issues of culture and human rights, Nour is advancing initiatives in international women's health.

Previous recipients of the MacArthur "genius" grants include David C. Page '82 and Paul Farmer '90. Page, a molecular geneticist and associate director of science at the Whitehead Institute in Cambridge, Massachusetts, received the fellowship in 1986 for his research on how genes on the sex chromosomes lead to male or female development. Farmer, the Maude and Lillian Presley Professor of Social Medicine at HMS, was granted a fellowship in 1993 for his work as a physician, anthropologist, and community health activist. ■

The Next Hundred Years

IN SEPTEMBER, HARVARD MEDICAL SCHOOL CELEBRATED the 100th anniversary of the groundbreaking of its original Quadrangle and dedicated the New Research Building on the recently dubbed North Quadrangle. Since the alumni have played a significant role in shaping the campus over the past century, we were invited to join the festivities for this most recent defining moment in the history of our alma mater. For those who were not able to attend, I have included excerpts of my comments:

In the fifth century BC, Heraclitus noted, "Nothing endures but change." Throughout its history, Harvard Medical School has courageously met the challenges of change, sometimes with ease and occasionally with hesitation, but always with a spirit of determination and strong leadership. As a way of marking this celebration, I invite you to join me on a brief journey into the past and a visionary peek into the future.

talized student life at Harvard. Unknowingly, the alumni had engineered the construction of the first building on what we now call the North Quad—Vanderbilt Hall.

And so we celebrate the extension of the North Quad. Architecturally, this building embodies a new attitude for the School. In sharp contrast to the opaque, Greek-inspired marble exterior of the South Quad, the glass exterior of the new building bears witness to a spirit of collaboration and openness at HMS. It also reaffirms Dean Joseph Martin's symbolic reopening of the front door of Gordon Hall in 1997. Scientific investigation can no longer occur in the solitude of a single laboratory, but must involve a symphony of investigators, even on a global level. By welcoming the warm rays of the sun within its walls, HMS also welcomes the community and helps ensure that the research conducted in the building remains relevant to the human condition. Once again, Harvard is responding to the challenges

Scientific investigation can no longer occur in the solitude of a single laboratory, but must involve a symphony of investigators, even on a global level.

As I began preparing these remarks while at home in Baltimore, we were being visited by a stormy young lady named Isabel. It was appropriately by candlelight, then, that I found myself rereading Nora Nercessian's centennial account of the Harvard Medical Alumni Association, which began in 1891. In that monograph, Dr. Nercessian notes the critical involvement of the alumni in moving the campus from Boylston Street to Longwood Avenue, then a barren marshland.

The first president of the Alumni Association, James Chadwick, Class of 1871, reaffirmed the importance of the organization in lifting the standard of medical education. He and others were instrumental in raising the necessary funds to construct this fortress of knowledge and investigation. He also reaffirmed the importance of the School as part of a larger university, at a time when nationwide there was "a multiplicity of independent schools with no high motives."

The alumni helped lead the needed reform in medical education. And when it was apparent that the young men of Harvard were having difficulty finding decent lodging in Boston, the alumni helped establish the first medical school dormitory of its type in the country and the first realization of Harvard President A. Lawrence Lowell's vision for a revi

of a changing research landscape with determination and enlightened leadership.

I can imagine a scenario 100 years from now in which HMS is dedicating the groundbreaking of its third international campus—located in Beijing, perhaps—and the president of the Harvard Medical Alumni Association is in attendance, representing not just 900 alumni as Dr. Chadwick did, nor 8,800 as I do now, but more than 20,000 alumni, from such fields as stem cell and gene therapy, pharmacogenetics, and applied nanotechnology.

You may find that large number surprising, but keep in mind that the human life span will have expanded by 10 percent and that the continued efforts of HMS to recruit a diverse student population will have been extremely successful. And when the time capsule is opened and the award-winning 75th anniversary issue of the *Harvard Medical Alumni Bulletin* is retrieved, undoubtedly someone will remark, "So *those* are the ones who shaped our medical past and enabled us to navigate the constant changes in our medical landscape." ■

Eve J. Higginbotham '79 is chair of the Department of Ophthalmology at the University of Maryland School of Medicine.

Home Repair Books for Body & Soul

The Memory Cure: How to Protect Your Brain Against Memory Loss and Alzheimer's Disease, by Majid Fotuhi '97 (McGraw-Hill, 2003)

Everything You Never Wanted Your Kids to Know About Sex (But Were Afraid They'd Ask), by Justin Richardson '89 and Mark A. Schuster '87 (Crown, 2003)

THESE ARE HOW-TO TIMES, FULL OF HOME REPAIR BOOKS FOR body and soul. Enormous efforts go into writing them. They are meant to make our lives better, or at least more manageable. But advice books require time to read, lots of time—and lack of time is the broken light bulb most homes fail to fix.

Take *The Memory Cure*, by Majid Fotuhi '97. The magic claim comes on page three: "it's possible for you...to have a perfect memory for life." Who could turn that down? Fotuhi, according to his bio line, "has the unique distinction of being both a faculty member in neurology at HMS and a neurology consultant at the Alzheimer's Disease Research Center at Johns Hopkins Hospital." This will be good.

For the patient reader, there follow sections on stages and types of memory; one feels intelligent for knowing them. There are sections on the differences between age-associated memory impairment, mild cognitive impairment, and Alzheimer's dementia. There are sections on plaques, tangles, cholinergic cell death, and the sequential deterioration of temporal, frontal, and parietal lobes that occurs in Alzheimer's disease. For confused and despairing families just beginning the process of diagnosis, there is also a useful chapter on reversible dementias.

At last, Fotuhi comes to his Memory Protection Plan; the 401(k) of cognitive savings. I read the ten steps, reflected with some disappointment (no magic), then summarized them for my mother, who sat reading the Sunday paper on a couch across the room. I told her Fotuhi's advice: lower her blood pressure, control her cholesterol, check her B12 and homocysteine levels, add antioxidants to her diet, prevent skull injury, minimize sensory deficits, optimize exercise physically and mentally, socialize (promotes multi-lobe stimulation), and be happy (decreases cortisol levels). I waited for her response.

The target audience gestured for the book. I tossed it over. She glanced at the title and opened to the table of contents.

"How long is it?" she asked. She could use a cure.

"One hundred and seventy-seven pages," I replied.

"Too long," she said, snapping the book shut. "Hand me the *Times* magazine section."

With a different audience, on a separate topic, I tried to share another how-to book. *Everything You Never Wanted Your Kids to Know About Sex (But Were Afraid They'd Ask)*, by Justin Richardson '89 and Mark A. Schuster '87, is 379 pages long. Encyclopedically speaking, it is a full-alphabet tour of sexual development, parenting styles, and suggestions for unavoidable and pivotal situations through the life cycle: how to respond to early self-stimulation ("humping Barney"), how to anticipate puberty, how to discuss sexually transmitted diseases and birth control, how to consider the logistics of permissive sexual activity. These could be useful when a parent is caught blindsided—or is hoping not to be.

The second-person tone is determinedly friendly and happy-go-lucky; these are guys you could tell anything to—the neighbor who keeps all secrets, the favorite bartender. There are catchy study results—by three years old, 95 percent of boys have the word for their penises, but only 52 percent of girls have the words for their vaginas and vulvas; in a sample of American children asked about the purpose of sex, not one child under nine included pleasure; American kids can explain the mechanics of procreation by eleven years old, English kids by nine, and Swedish kids by seven.

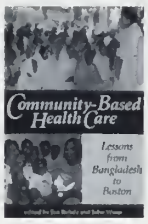
There are simple wisdoms, too: "authoritative parenting is about as close as science has come to offering a recipe for healthy kids," or, "nurturing your child's sexual development is no less bittersweet than any other aspect of her growing up." But all this is buried in many clever anecdotes about interactions between parent and child; by page 250, it's a little like looking at too many photos of someone else's family. Still, the intentions are clear, decent, and important.

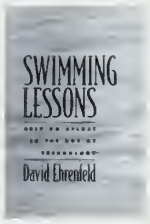
So I offered the book to a friend, a working mother with two kids rounding the corners of puberty. She glanced at its width, then handed it back as if it were hot. "Can they cut to the chase?" she asked. "Mothers don't have time to read."

This is the essential problem. There is so much in this world we ought to know, think, prepare for, and practice to prevent. Doing so would make life infinitely better. But this same life, the one full of timesaving technologies, has left most of us forlorn from lack of time by the end of each day. We are not free to read long and useful books. We have to wait for the tapes. ■

Elissa Ely '88 is a lecturer on psychiatry at HMS.







The Healing Art

A Doctor's Black Bag of Poetry, by Rafael Campo '92 *(W. W. Norton and Company, 2003)*

An advocate of tapping into the power of language to help people heal, Campo explores the strong medicine offered by a range of acclaimed poets, including William Carlos Williams, Mark Doty, and Audre Lorde. Campo reflects upon his patients' positive responses to "poetry treatment" and suggests a biocultural model of illness that would integrate the needs of the body, mind, and soul.

Pathologies of Power

Health, Human Rights, and the New War on the Poor, by Paul Farmer '90 *(University of California Press, 2003)*

In his 20 years as an anthropologist and physician in Haiti, Peru, and Russia, Farmer has witnessed the struggles and suffering of people confronting illness in extreme situations. He recounts their stories to promote a deeper understanding of human rights, linking individuals to the larger picture of political and economic injustice.

Passive-Aggression

A Guide for the Therapist, the Patient, and the Victim, by Martin Kantor '58 *(Praeger Publishers, 2002)*

Kantor's book on the controversial subject of passive-aggressive personality disorder provides detailed clinical descriptions of the passive-aggressive patient, the victims of passive-aggression, and the interaction between the two. Kantor also describes a treatment approach using several therapeutic methods—psychodynamic, supportive, cognitive, behavioral, and interpersonal—to help patients deal with anger in a healthier way.

Community-Based Health Care

Lessons from Bangladesh to Boston, edited by Jon Rohde '67 and John Wyon *(Management Sciences for Health, 2002)*

In this anthology, 36 of the world's leading health experts reflect on their experiences in poor communities worldwide. The contributors explore such issues as equity, health financing, home visiting, and community-based health information systems as they recount their attempts to improve health care in countries as diverse as India, Peru, Haiti, Vietnam, and the United States.

Complications in Ophthalmic Plastic Surgery

edited by Brian G. Brazzo '92 *(Springer, 2003)*

This new volume instructs surgeons on how to prevent and manage the most common and significant complications associated with ophthalmic plastic surgery. Contributions from a number of oculoplastic surgeons are organized into three parts—Cosmetic Surgery, Ptosis, and Lower Eyelid Manipulation—and each chapter includes sections on evaluation, technique, and complications.

Swimming Lessons

Keeping Afloat in the Age of Technology, by David Ehrenfeld '63 *(Oxford University Press, 2002)*

Trained in history and zoology as well as medicine, Ehrenfeld examines the effects of environmental degradation on human potential and considers new developments in such areas as education, military weapons systems, and biotechnology. He reveals how corporate economic practices affect the way we live, work, and relate to each other, and offers suggestions to help people remain connected to nature and to restore damaged communities.

True Blue

A Novel, by Jeffrey Lee '87 *(Delacorte Press, 2003)*

The author, a family physician, has written a novel for young adults that explores what it means to be different. When Molly, the new girl in school, meets Chrys, she's drawn to his quiet, mysterious manner. Soon the two become partners to try to win the school science competition, and an unlikely friendship develops. As they work on their project, they reveal secrets to each other and learn to value their own unique gifts.

Harry Potter and the Changer of Secretions

UPON ENTERING THE HOGWARTS School of Witchcraft and Wizardry, Harry Potter discovers a mysterious world filled with gigantic talking spiders, chess pieces that come alive, and a slathering three-headed dog named Fluffy. Soon enough, he gains admission to an even more mystifying realm—puberty, one of the most perplexing stages in the human life span. Now researchers have identified a gene, GPR54, that appears to play a critical role in the onset of puberty, and they've dubbed the gene Harry Potter after the boy wizard.

Adolescence begins when the hypothalamus, at the apex of the reproductive axis, sends out sharp pulses of gonadotropin-releasing hormone (GnRH). Reproductive biologists still have not pinpointed the molecular players that allow the hypothalamus to transmit its puberty-inducing signal. But Massachusetts General Hospital scientists, working with researchers at other institutions, have discovered that GPR54 appears to play a critical role in getting out the message.

Stephanie Seminara, William Crowley, and colleagues were first alerted to the role of GPR54 when they discovered a mutant version of the gene in people with idiopathic hypogonadotropic hypogonadism (IHH). Unless treated, males with IHH fail to virilize—their voices do not deepen and their muscles and testes do not enlarge. Females neither menstruate nor develop normal breasts.

Working with colleagues at Paradigm Therapeutics, a small biotechnology firm, the researchers found that mice lacking the GPR54 homologue exhibit symptoms of IHH. So compelling is the story that the *New England Journal of Medicine* broke a longstanding policy of publishing only clinical research; the article appears in its October 23 issue. "This is the first time the *Journal* is publishing animal data, a historic event," says Seminara, HMS assistant professor of medicine.

The role of the GPR54 protein is to get the GnRH message out of the hypothalamus, rather than to synthesize the hormone. Seminara and her colleagues found that mice lacking GPR54 have normal levels of GnRH in their hypothalami. When injected with exogenous GnRH, the mice's pituitary glands, the next step along the reproductive axis, responded. "So the problem," Seminara says, "is in either the processing or the release of GnRH from the hypothalamus."

PHOTO: GRAHAM GORDON RAMSAY

DECODING RING: Massachusetts General Hospital researchers—including, from left, William Crowley, James Acierno, Jr., and Stephanie Seminara—helped solve the mystery of a gene related to puberty.

IHH patients can be launched into puberty by pulsatile GnRH injections—a method pioneered by Crowley, HMS professor of medicine, nearly 25 years ago. The GPR54 discovery could lead to more sophisticated treatments for IHH and other diseases. "There are a number of disease models—relating to puberty, hormone-dependent cancers, endometriosis—where you either want to stimulate or, more often, downregulate the reproductive axis," Seminara says, "and GPR54 might provide the first clue toward developing therapies."

That such an important clue should lie with GPR54 would have struck many as unlikely a few years ago. Identified in 1999, the associated protein was little understood, other than that it was a G protein–coupled receptor with an affinity for metastasin, a metastasis-suppressing ligand. "The literature about GPR54 was more in the cancer field," says Seminara. And there it might have stayed had Yousef Bo-Abbas, a former postdoctoral fellow in Crowley's laboratory, not discovered, in his native Kuwait, a Saudi Arabian family with a large pedigree of IHH.

Seminara, Crowley, and their colleagues used genetic linkage analysis to scour the family's chromosomes for defective genes. The researchers narrowed their search to the short arm of chromosome 19, then, using human genome maps, to a handful of genes. GPR54 caught their eye mostly because of the intriguing distribution of its protein—it appeared in the brain, pituitary, and placenta. "It had a bit of an endocrine feel to it," Seminara says.

As it turned out, GPR54 was defective not just in the Saudi family, but also in a patient that Seminara and her colleagues had seen in the clinic at Massachusetts General Hospital. They had begun experiments to figure out how the defect was disrupting this patient's sexual maturation when Seminara received a telephone call from Stephen O'Rahilly, a member of the advisory board of Paradigm Therapeutics. The company had just produced a knockout mouse that reproduced many of the symptoms of IHH. "He said to me, 'Stephanie, the mouse gene's human homologue resides in your region of chromosome 19,'" Seminara says. "He

did not say the name of the mouse gene and I did not say GPR54, but we both knew. It was a wonderful moment."

Not only did the mice reproduce symptoms of IHH, but their pituitary glands also responded positively to GnRH injections. It was only after the researchers dissected the mouse hypothalami that they found direct evidence of the GPR54 protein's possible role as exporter, rather than synthesizer, of GnRH. "We found the GnRH content of the hypothalamus was normal," Seminara says. "That was the most powerful element of the data."

Many hormones are clipped and cleaved to reach their final form. It is possible that the mice's lack of GPR54 may interfere with that process. "We do not know exactly what form of GnRH was sitting in the hypothalamus of the mice," Seminara says. "It is also possible that GnRH is processed completely fine and is just not getting out."

Seminara and colleagues will be exploring yet another intriguing option. Although the hypothalamus triggers puberty by sending out intense pulses of GnRH, lower levels are released all along. During embryonic development, waves of GnRH wash through the reproductive axis. They are greatly subdued soon after birth, but the pulses never completely disappear. "GPR54 could be involved in the same system that is involved in the quieting of the axis after the first few months of life," Seminara says. "It could be involved in the pubertal reawakening of the reproductive axis."

Paradigm Therapeutics gave GPR54 the nickname "Harry Potter" following its tradition of naming knockout genes after famous orphans. Yet it may be only a matter of time before further studies illuminate the precise role of this mysterious gene. ■

Misia Landau is the senior science writer for Focus.

MEMORIES ARE MADE OF THIS

SCIENTISTS KNOW THAT SLEEP IS NECESSARY FOR GOOD MEMORY RETENTION, but new reseorch indicotes thot three stoges of waking and sleep time may determine how occurately motor-skill memories are recalled. The findings could help stroke and head injury patients more efficiently relearn how to walk, talk, and otherwise move.

In the October 9 issue of *Nature,* Matthew Wolker, an HMS instructor in psychiotry ot Beth Israel Deoconess Medicol Center, reports his investigotion of motor-skill memory, in which eight groups leorned finger-topping sequences similar to a piano exercise. Each group had a different schedule for being awake, sleeping, ond recalling the sequences.

Working in colloborotion with Robert Stickgold, on HMS ossistont professor of psychiatry ot the Mossochusetts Mentol Heolth Center, Wolker onalyzed how quickly and accurately the groups performed the sequences ond noted that three stages were necessary for the best memory recall. He compares these stages to the different processes a computer goes through to establish a file.

The broin first initiates a memory much as a computer creates a document file. To save the memory, the brain needs about six waking hours for processing. If the computer shuts down or the broin goes to sleep before the file is properly soved, it is lost.

According to Walker, the second stoge "is obsolutely dependent on sleep in order to occur." During a good night's sleep, the broin edits the memory file and mokes it more efficient. This editing process requires several hours of sleep. "If you don't get that full night's sleep, you may be shortchanging your brain of learning potential," soys Walker.

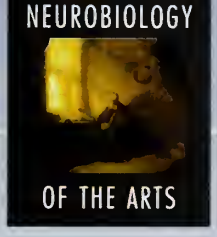
The finol stoge is the "recall phase," in which a saved, edited memory becomes usable. "After the memory had been stabilized and enhanced, it once agoin become pliable so thot it could be altered in the context of new ongoing experiences," Wolker says. This stoge allows the brain to tweak ond perfect previously leorned skills.

Walker says the lost stage may explain why some potients with posttraumatic stress disorder benefit from talking about their experiences. As the potients recall their traumos, their memories are slightly altered. "Over time," he says, "there may be the chance for these potients to redefine their memories ond moke them less traumotic." ■

—Nicole Giese

MONET ISN'T EVERYTHING: Louis Leroy found Monet's *Impression, Sunrise* "vague and brutal" and "worse than anyone hitherto had dared to paint."

light



Why do Monet's poppies stir in the breeze? Why does Mona Lisa's smile disappear, then reappear, as our gaze shifts? A neurophysiologist reflects on how our visual processing system affects our perceptions of art.

by MARGARET LIVINGSTONE

VISION

WHEN THE ART CRITIC LOUIS LEROY ATTENDED a new Paris show in the spring of 1874, he expected to see "the kind of painting one sees everywhere, rather bad than good, but not hostile to good artistic manners." Instead, he found a "hair-raising exhibition" whose nadir was Claude Monet's *Impression, Sunrise.* Leroy pronounced the seascape "at once vague and brutal" and "worse than anyone has hitherto dared to paint." Despite his revulsion—and that of many of his contemporaries—history has acknowledged this painting: from Leroy's sneering review came the name for the art movement Impressionism. But what made Leroy object so fervently?

The answer may lie in part with the painting's luminance, or perceived lightness. The elements of visual art have long

IMAGE COURTESY OF RÉUNION DES MUSÉES NATIONAUX/ART RESOURCE, NEW YORK

Most people are comfortable talking about color. Yet luminance, even though it is more fundamental, is dimly understood.

IMAGE COURTESY OF RÉUNION DES MUSÉES NATIONAUX/ART RESOURCE, NEW YORK

PRODIGAL SUN: The sun in *Impression, Sunrise* (top) appears so brilliant that it seems to pulsate. But a grayscale version reveals that the sun is actually no lighter than the background clouds. To the more primitive subdivision of our visual system, the sun appears almost invisible in the painting. In the bottom version, the sun has been made lighter than in the original—which is closer to the way it would appear in reality—and it now seems, paradoxically, less bright.

been held to be color, shape, texture, and line. But an even more basic distinction lies between color and luminance. Color can convey emotion and symbolism, but luminance alone defines shape, texture, and line. "Colors are only symbols," Pablo Picasso once wrote. "Reality is to be found in lightness alone."

Most people are comfortable talking about color. Yet luminance, even though it is more fundamental, is dimly understood. Given two patches of gray, it is easy to identify which is lighter, but given two colors, it is often difficult to draw such a distinction.

A monochromatic rendering of *Impression, Sunrise* reveals that Monet painted the sun at exactly the same luminance as the gray of the clouds. If he had rendered it in a strictly representational style, the sun would have been brighter than the sky by a factor too large to have been duplicated with pigments. If he had made the sun lighter—which is closer to the way it would appear in reality—it would have lost its quavering luminosity and would have seemed, paradoxically, less bright. Rather than appearing as a source of light, the sun would have looked like a cutout affixed to the clouds. By rendering the sun the exact luminance as the sky, Monet achieved an eerie effect: his orange sun appears to pulsate across the grayish-green water.

Gray Matters

Color and luminance play distinct roles in our perception of art—and even of real life—because our visual systems analyze color and luminance separately. The areas of our brain that process information about color, in the temporal lobe, are several centimeters away from the areas that analyze luminance, in the parietal lobe. They are as anatomically distinct as vision is from hearing.

The luminance system, which is evolutionarily older, is common to all mammals; the parts of the brain that process color information are present only in primates. That is probably why the most primitive visual information about a scene is found in variations of luminance. It does not matter which color is used to convey the luminance signal, because the parts of our brains that analyze the most basic features of a scene are, quite literally, colorblind.

On a gross level, the visual system is a single pathway in the brain. On a finer scale, however, this pathway consists of two major subdivisions. The evolutionarily older large-cell subdivision is responsible for our perception of motion, space, position, depth, figure-and-ground segregation, and the overall organization of the visual scene. This subdivision is called the "Where" system. The small-cell subdivision, which is well developed only in primates, is responsible for our ability to recognize objects, including faces, in color and in complex detail. This newer system is called the "What" system.

The Where and What systems differ not only in the kind of information they extract from the environment, but also in how they process light signals. The Where system is colorblind; the What system carries information about color. The Where system has a much higher sensitivity to small differences in brightness. It is also faster and more transient in its responses and has a slightly lower acuity, or resolution. In the retina, thalamus, and early cortical areas, the Where and What systems are physically interdigitated, yet they keep the information they process largely separate. At higher levels, the two subdivisions become even more spatially segregated.

Evolution likely accounts for these subdivided visual tasks. The Where system in humans and other primates resembles the entire visual system of

BLACK AND BLUE: The melancholy blues in Pablo Picasso's *The Tragedy (Poor People on the Seashore)* carry the emotional content of the painting. But a black-and-white reproduction reveals that it is not the colors themselves but their luminance that makes it possible for us to recognize the figures, to perceive their three-dimensional shape, and to understand the spatial organization of the scene.

lower mammals. These animals are much less sensitive to color than we are, and they can neither scrutinize objects nor accurately discriminate them on the basis of visual attributes. Instead they are sensitive to objects in motion, because things that move—whether prey or predator—are likely to be important.

Also, because the primitive visual system must have been used to navigate through three-dimensional environments, it had to have been able to process depth information and distinguish objects from their backgrounds. As the more complicated primate visual system evolved, the original system was maintained, probably because it was simpler to overlay color vision and object recognition onto the existing system than it would have been to integrate the two.

Artistic License

In the first and most fundamental step of our visual processing, our retinal ganglion cells are excited by light impinging on their receptive field centers. Notably, however, they are inhibited by light falling on the immediately surrounding region. The net effect is to record the relationship of "center" to "surround."

Cells at the next stage of processing, in the thalamus, show a similar center/surround organization, which makes cells at these early stages of the visual system sensitive to discontinuities in the pattern of light falling on the retina rather than to the absolute level of light. Neurons respond best to sharp changes, rather than to gradual shifts in luminance. This wiring allows the visual system to ignore gradual changes in light and the overall level of the illuminant, factors that are usually not important biologically. Many visual modalities—such as luminance, color, motion, and depth—exhibit greater sensitivity to abrupt than to gradual change. In each modality, this selectivity is due to an underlying center/surround organization.

It makes adaptive sense for our visual system to be designed in this way because it is more efficient to encode only those parts of the image that have changes or discontinuities than to encode the entire image. The visual system in a sense compresses images because it takes energy for nerve cells to signal; the fewer cells that signal, the more energy is conserved. Higher-level visual processing, such as object recognition, is essentially the end result of extracting the information content of an image.

Artists can take advantage of this quirk in our visual system to expand the apparent range of reflectances of paints. Although a real scene may contain a large spectrum of luminances, our visual system initially analyzes each part of the scene separately. So by introducing gradual changes in the background luminance, for example, an artist can shift the apparent luminance of the foreground in the opposite direction.

Tricks of the Light

Artists have been playing with luminance for centuries. In his 1632 painting *Meditating Philosopher,* Rembrandt used variations in luminance to create an almost ethereal golden glow. If this were a real scene, the luminance of the window would likely be hundreds of times that of the upper reaches of the shadowy staircase—an effect nearly impossible to duplicate with paint alone. The paint representing the window actually reflects only 15 times more light than the paint representing the shadows in the lower left corner of the painting, but we perceive the window section to be substantially lighter.

FOOL'S GOLD: In Rembrandt's *Meditating Philosopher,* the point representing the window reflects only 15 times more light than the point representing the shadows in the lower left corner, but we perceive the window section to be substantially lighter. By using a combination of gradual background changes and local abrupt changes in luminance, Rembrandt simulated a much larger range of luminances than his pigments could supply.

IMAGES COURTESY OF THE NATIONAL GALLERY OF ART/©2003 ESTATE OF PABLO PICASSO/ARTISTS RIGHTS SOCIETY (ARS), NEW YORK (PICASSO); COURTESY OF RÉUNION DES MUSÉES NATIONAUX/ERICH LESSING, ART RESOURCE, NEW YORK (REMBRANDT)

Some of the color combinations the Impressionists used have so little luminance contrast that they create the illusion of motion.

Rembrandt created another illusion by painting the philosopher's head on a darker background and the crosspiece of the window frame on a lighter background. The head thus appears relatively light and the window frame relatively dark, even though the head is darker than the frame. We cannot easily perceive the differences in the backgrounds because they meld gradually into one another. By using a combination of gradual background changes and local abrupt changes in luminance, Rembrandt simulated a much larger range of luminances than his pigments could supply.

Over the centuries, artists continued to increase their command of luminance to enhance their ability to represent depth on a two-dimensional canvas. This trend toward representationalism reached a pinnacle in the early nineteenth century with the work of Jean-Auguste-Dominique Ingres, whose paintings have an amazingly photographic quality. Art historians have suggested that Ingres must have used a camera lucida or other optical aid to project an image of the scene onto the canvas or drawing tablet, so uncannily does he capture the gradations of luminance in his subjects.

Then, toward the end of the nineteenth century, the Impressionists aligned themselves against the representational style of art epitomized in the work of Ingres. Some experimented with color and luminance, sometimes using unrealistic color gradations or abandoning luminance differences entirely.

IMAGE COURTESY OF FRANCIS G. MAYER/CORBIS

PHOTO FINISH: In many of his paintings, such as the *Comtesse d'Haussonville*, Ingres took the command of luminance to a new level, with more detail in the shadows of his paintings than in some of the sharpest photographs.

Still Lifes in Motion

One of the Impressionists' most novel accomplishments is the shimmering, alive quality they achieved in many of their paintings. The sensation of movement in *Impression, Sunrise*—and some of Louis Leroy's disdain for the painting—stemmed in part from Monet's use of quick dabs of paint, which required the viewer's eye to blend the colors. "Wallpaper in its original state is more finished than this seascape!" Leroy groused.

And yet it is clear that some of the color combinations the Impressionists used have so little luminance contrast that they create the illusion of motion. We perceive illusory motion in images made from equiluminant colors for the same reason we don't see appropriate depth in these images: our Where system can't distinguish between equiluminant colors. Therefore if an image is composed of equiluminant colors, our What system can see those objects, but our Where system—which is responsible for our ability to see motion and position, as well as depth—cannot register their position and stability, so they can seem to jitter.

Monet's *The Poppy Field Outside of Argenteuil* is a good example of this illusion. The red of the flowers is nearly equiluminant with the green of the grass and the skirt of the woman in the foreground. Our color-selective What system can easily distinguish the poppies and the skirt from the grass. But the colors, although bright, do not have enough luminance contrast for our Where system to see them. Their position seems uncertain, giving them an illusory instability. They can seem to move, as if stirred by a breeze.

Our eyes can be similarly tricked by repetitive high-contrast lines, which tend

LEVELING THE FIELD: In Monet's *The Poppy Field Outside of Argenteuil*, the red flowers, green gross, ond purple skirt ore opproximotely equiluminont. Becouse our "Where" system connot see them cleorly, their position seems uncertoin. They con seem to move, os if stirred by o breeze.

to create motion perpendicular to their own orientation. Light shining through horizontal venetian blinds, for example, will induce the appearance of vertical motion on an adjacent wall, a phenomenon known as the McKay illusion.

An extreme example of this illusion is Isia Leviant's *Enigma*. The juxtaposition of luminance-contrast borders with areas of equiluminance can cause the illusion of motion; after looking at *Enigma* for a minute or so, the viewer should notice a streaming effect in the colored circles. The streaming always moves perpendicularly to the high-contrast lines, which induce it. We do not yet understand why a large field of high-contrast lines induces an illusion of motion. Some of Monet's paintings likely induce a mild form of this deception to help create their illusory sense of movement.

Art Mystery

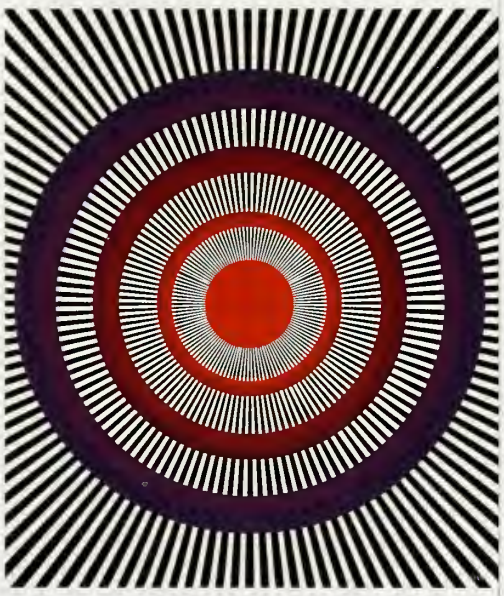
Five hundred years after Mona Lisa sat for Leonardo da Vinci, we're still trying to understand what makes her painted image so lifelike. She seems to smile until you look at her mouth, then her smile fades, like a dim star that disappears as soon as you gaze directly at it. One popular idea is that Leonardo used sfumato—a technique of subtly blurring sharp outlines—to make her expression ambiguous. That hypothesis would mean that her smile would vary depending on the viewer's imagination or state of mind, but its variability is more systematic than that.

While looking at the painting one day, I noticed that Mona Lisa's expression changed according to how far the center of my gaze strayed from her mouth. These systematic transformations suggested that her lifelike quality was not so mysterious after all. Her smile, I realized, is differentially apparent in different parts of our visual field.

To understand how Mona Lisa's smile would look at a range of eccentricities, I processed images of her face to reveal its fine, medium, and coarse components. A clear smile is more apparent in the coarse and medium components of the images than in the fine detail image. This means that if the center of your gaze falls on the background or on Mona Lisa's hands, her mouth—which is then seen by your peripheral, low-resolution vision—appears cheerful. When you look directly at her mouth, your high-resolution foveal vision sees details that take away the grin. This explains the elusive quality of her expression: you literally can't catch her smile by looking at her mouth.

The spatial imprecision of our peripheral vision has interesting implications for our perception of some Impressionist paintings, too. In Monet's *Rue Montorgueil in Paris, Festival of June 30, 1878*, for example, details are spatially jumbled. If you look carefully at the flags just to the left or right of the center of *Rue Montorgueil*, you can see that the blue, white, and red brushstrokes, representing the stripes of the tricolored flags of France, are not always well aligned or even adjacent to one another. This spatial imprecision differs from a simple blurring: it mimics the spatial imprecision in our peripheral visual field.

Our peripheral vision occasionally makes erroneous correlations between objects seen and objects known to exist. This phenomenon, called illusory conjunction, occurs when items are presented either peripherally or transiently. The flags along the Rue Montorgueil look fine when you first glance at the painting, but not if you look directly at them, or after you study those parts specifically. The painting's spatial imprecision is



SPINNING WHEEL: In Isio Leviont's *Enigmo*, the juxtoposition of luminonce-contrast borders with areos of equiluminonce con couse the illusion of motion; ofter gozing at the painting for even o moment, the viewer should notice o streoming effect in the colored circles.

Artists must learn to see luminance gradation and to evaluate
Even then, they often find it impossible to duplicate those

IMAGE COURTESY OF RÉUNION DES MUSÉES NATIONAUX/ART RESOURCE, NEW YORK

LOOSE LIPS: Mona Lisa's expression changes depending on how far the viewer's center of gaze is from her mouth. A clear smile is more evident on her face in details that show the coarse and medium image components (left and center) than in the one that shows only fine details (right).

not immediately noticeable because our own spatial imprecision allows illusory conjunctions to complete the objects. That explains why we see complete flags, even though many of them are just single strokes of paint.

Low spatial precision can lend vitality to a painting, because our visual system fills in the picture differently with each glance. It also gives the painting a transient feel because such imprecision is compatible with a single glance, a fleeting moment in time. Because of the low spatial resolution of peripheral vision, we cannot take in a detailed percept of the entire scene in a single glance; we see clearly only the part of the scene that our center of gaze happens to light on. "The visual sensation that imprints itself on the retina lasts but a second, or even less," wrote Impressionist painter Gustave Caillebotte, a master of the art of capturing a fleeting moment. "That's the impression that we had to pursue."

By comparison, Nicolas Poussin's highly detailed, action-packed *Rape of the Sabine Women* looks relatively static, because we can see hundreds of details. Seeing so many details is incompatible with the transience of the incident depicted—by the time our eyes move from one act of savagery to another, the scene should have changed. The longer you look, the colder and more frozen the figures in the painting seem.

In the Shade

When a light source illuminates a three-dimensional object, different parts of the object's surface reflect different amounts of light, depending on the angle of the light hitting them. We see these differences as changes in luminance, or shading, which is another depth cue that, like perspective, artists must learn to render.

To use shading effectively, artists have to surmount several challenges. They must learn to see luminance gradation and to evaluate luminance independent of color. Even then, they often find it impossible to duplicate those luminance ranges with pigments because of the limited range of reflectances available even with the best paints. The range of luminances in a given scene is almost always far greater than the array of values an artist can achieve using pigments. Inside a typical room, for example, luminances vary widely: a light source, such as a window or lamp, might be hundreds of times brighter than the shadowed region under a desk. The luminance in outdoor scenes usually varies by a factor of a thousand.

We know that luminance contrast, not color, is necessary for depth perception. A corollary of this principle is that, as long as you have the appropriate luminance contrast, you can use any hue you want and still portray a shape in three dimensions with shading. In Henri Matisse's *La Femme au Chapeau*, for example, the shadows and most of the planes of the subject's face are peculiar colors. Although it is difficult to imagine what kind of lighting would cast blue and mauve shadows, the three-dimensional shape of the woman's face does not seem

luminance independent of color. luminance ranges with pigments.

unnatural because the patches of bizarre colors have the correct relative luminance to represent planes and shadows. Matisse himself explained, "While following the impression produced on me by a face, I have tried not to stray from the anatomical structure."

Matisse had discovered that he could use any hue and still portray the three-dimensional shape he wanted as long as the luminance was appropriate. The art collector Leo Stein, who eventually bought the painting, wrote, "It was a tremendous effort on his part, a thing brilliant and powerful, but the nastiest smear of paint I had ever seen."

A Double Take

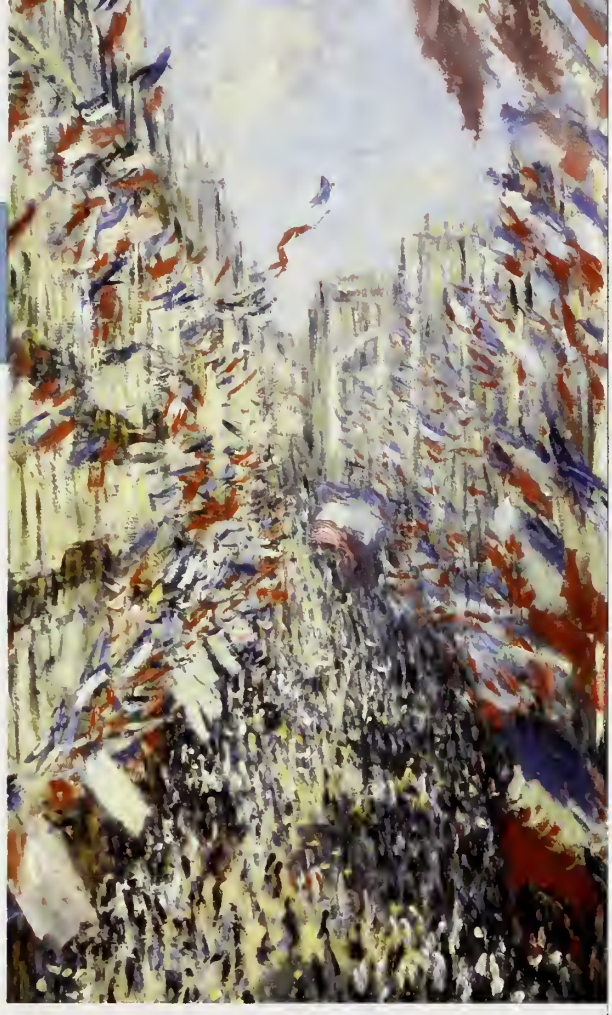
Although late Renaissance painters attained a photographically realistic use of perspective and shading, those techniques alone could not convey an authentic feeling of three-dimensionality. No matter how convincingly an artist renders shading and perspective, two other important cues—stereopsis and relative motion—inform the viewer's brain that the painting is, in fact, flat.

Since our two eyes view the world from slightly dif ferent positions, the images on the two retinas differ slightly. Stereopsis is the ability of our visual system to interpret the disparity between the two images as depth. A stereoscope, a device popular in the mid-nineteenth century, presented two slightly different pictures, one to each eye, to give a vivid sense of depth. The View-Masters many of us enjoyed as children also work on this principle, showing three-dimensional images of pterodactyls, volcanoes, and Donald Duck.

The same part of the brain that codes stereopsis codes depth from relative motion, so movements as small as the distance between our eyes are large enough to produce a strong depth signal. We glean information about distance from the relative motion of objects as we move past them. When you walk down a street at night, for example, the objects close to you, such as the trees along the sidewalk, seem to pass more quickly than the houses or trees farther away. Those at even greater distances, such as the moon, seem stationary.

We also pick up relative movement cues from the small head motions we make even when we stand still in front of a painting. No matter how skillfully the artist conveys depth through the use of perspective and shading, because the images in our two eyes are identical and because there is no relative movement between objects in the painting, our brains register the painting as flat.

The Impressionists found multiple ways to trick our brains, though. In most Impressionist paintings, cues such as perspective or shading, rendered in luminance contrast, convey a sense of depth. The blurriness and deliberate lack of details characteristic of many Impressionist paintings also contribute to a sense of three-dimensionality. To see stereoscopic depth, the image needs to



UNFLAGGING ENERGY: The spotiol imprecision in *Monet's Rue Montorgueil in Poris, Festivol of June 30, 1878,* generotes vitolity becouse it is consistent with o single glonce, o moment in time.

FREEZE FRAME: Nicolos Poussin's *The Rope of the Sobine Women* depicts o greot deol of oction, yet it seems more stotic thon Monet's *Rue Montorgueil* because our visuol system connot register so mony detoils ot once.

IMAGES COURTESY OF REUNION DES MUSEES NATIONAUX/ART RESOURCE, NEW YORK (MONET); THE LOUVRE/ERICH LESSING, ART RESOURCE, NEW YORK (POUSSIN)

IMAGE COURTESY OF SAN FRANCISCO MUSEUM OF MODERN ART © SUCCESSION H. MATISSE, PARIS/ARTISTS RIGHTS SOCIETY

HAT TRICK: Despite its odd colors, the shape of the woman's face in Matisse's *La Femme au Chapeau* seems natural because the relative luminance of the pigments is appropriate, even if the hues are not.

be detailed enough to allow us to detect the slight differences between our two eyes' images. By eliminating some spatial details and blurring others, an artist can hinder stereopsis from revealing the flatness of the image. This allows other depth cues in the painting, such as shading and perspective, to produce a more powerful signal because they are not as strongly contradicted by stereopsis.

The notable ability of some Impressionist and Post-Impressionist paintings to invoke an illusion of depth, or a sensation of atmosphere, also likely arises from the rendering of semiregular patterns of leaves or flowers, or even from coarse brush strokes. *Rue Montorgueil*, for example, produces an illusion of depth because of the semirepetitive patterns of the flags. Ironically, this effect goes beyond what realism could achieve—short of making two slightly different paintings and using stereo viewers—to generate a sense of depth.

The sense of atmosphere is particularly striking in Pierre-Auguste Renoir's *A Girl Gathering Flowers*. The dabs of paint can be mismatched in the images in our two eyes, giving the painting an illusory sense of a three-dimensional volume filled with small floating elements, such as flower petals, insects, and pollen.

Vision Quest

The ways in which we process color and luminance hold ramifications for more than paintings; they also affect our perceptions of television, computer graphics, photography, color printing, and movies. These technologies are all flat, like painting, so they use the same kinds of cues—perspective, shading, and occlusion—to give an illusory sense of

The higher levels of the "Where" system are located above the ears, in the parietal lobe, and the higher levels of the "What" system are located in front of the ears, in the temporal lobe. Because these areas are distinct, people can experience damage—from stroke or injury—to one system without the other being at all affected.

When the Where system is damaged, people have trouble locating objects; they have difficulty perceiving motion and depth, distinguishing right from left, and seeing complex objects in their entirety. Much of our knowledge of the function of the Where system comes from neurological studies of people who have sustained damage to the parietal lobe, such as Zasetsky, a Russian soldier who suffered a bullet wound to his left parietal area during World War II.

After his injury, Zasetsky described his vision as being severely disorganized and spatially fractured, though his recognition of individual objects was unimpaired. He had trouble grasping objects that he could plainly see because they would turn out to be to one side or the other of where he perceived them to be. He could not tell right from left, and he could see only one small part of an object or a scene at a time. His world would "glimmer fitfully and become displaced, making everything appear as if it were in a state of flux."

The neurologist Josef Zihl has described a stroke victim whose world, unlike Zasetsky's frenetic universe, appeared strangely static. Bilateral damage to her parietal lobe had affected her motion perception. She found herself in danger crossing streets because she could not judge the speed of approaching cars. "When I'm looking at the car first, it seems far away," she reported. "But then, when I want to cross the road, suddenly the car is very near." She eventually learned to gauge the distance of approaching vehicles by their sound. For this patient, even pouring a cup of tea was tricky, because she could not perceive the rising level of the tea in the cup. Midair, the stream of fluid appeared frozen, like a glacier.

When people suffer damage to the What system, they have trouble recognizing objects, animals, people, or colors. These visual losses can be surprisingly specific, indicating a high degree of functional specialization. With some kinds of stroke, for example, people can lose the ability to recognize colors but not the ability to recognize objects, or vice versa—evidence that the What system is further subdivided into a color system and a form system.

The process of object recognition must also be further subdivided, because strokes can occasionally result in uncannily specific losses of object recognition abilities. Some patients may retain a capacity to recognize living things only, for example, or lose their ability to identify fruits and vegetables. Not uncommonly, small lesions in the temporal lobe can result in a selective loss of the ability to recognize faces but not any other kind of object.

Neurologist Oliver Sacks has written about an artist whose injury had caused him to lose only his color perception; his other visual

brain teaser

depth. They also have the same problem as paintings in that our stereopsis regis ters the images as flat.

But movies and television have the potential for a powerful additional depth cue—relative motion. If you close one eye and gaze steadily at, say, the edge of this magazine, you may find that it does not seem clearly in front of background objects. But by moving your head slightly from side to side you can make it jump back into proper apparent depth. That is because relative motion of objects at different distances is a strong cue to their distance from the observer. Relative motion of objects in movies and television can be a powerful cue to depth and can even induce an illusion of being propelled through space. Who didn't have to grip their seat the first time they saw the opening credits for *Star Wars*?

Recent advances in our understanding of the human visual system allow us to look at art—and our perceptions of the world—in new ways. Without understanding the underlying neurobiology of color and luminance recognition, artists, advertisers, psychologists, and the technology industry have discovered various phenomena that turn out to be based on the parallel organization of our visual systems. It will be interesting to see whether an explicit understanding of the neurobiology of vision will lead to more sophisticated effects and illusions and a greater knowledge of brain function in general. ■

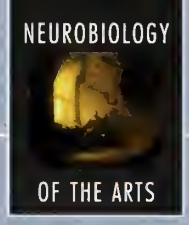
Margaret Livingstone, PhD, is a professor of neurobiology at Harvard Medical School. This article was largely adapted from her book Vision and Art: The Biology of Seeing, *published by Henry N. Abrams, Inc. in 2002.*

FLORAL REARRANGEMENT: The dobs of point in Renoir's *A Girl Gothering Flowers* can be mismotched between our two eyes, leading ta a pawerful sensotion of o three-dimensionol volume filled with small floating objects.

obilities remoined intoct. The ortist wos still oble ta recognize ond render objects, but his entire world—even the world he saw while thinking ond dreaming—became gray and drab. He was prafoundly disturbed by the wrangness of the oppeoronce of everything oround him. People resembled "animoted groy stotues," ond he found their groy flesh so obhorrent he began to shun them. Faad laoked so disgusting thot he had ta clase his eyes ta eat. Finally, he began ta consume only achromatic foods, such as black olives ond white rice.

Same peaple with temporol lobe lesions thot interfere with the Whot system con occurotely capy drawings af objects withaut having the slightest idea what those objects are. Others with a lesian in a slightly different part af the temparal labe cannat recagnize faces that had once been familiar, such os those of fomily members, friends, or celebrities. One mon who hod suffered a stroke told his doctor, "I con see the eyes, nose, and mouth quite clearly, but they just dan't add up." At his sacial club ane day the strake victim naticed thot a stranger kept staring ot him; when he finally asked the steward who the ill-monnered bloke wos, he leorned thot he hod spent the afternoon gozing ot himself in a mirror. ■

REPRODUCTION ISSUES: As port of o vision test, Oliver Socks osked two of his potients to try to reproduce the imoge in the left ponel. The center ponel shows o reproduction mode by o red/green colorblind person; the right ponel shows o reproduction mode by a mon with o lesion in the color processing port of his broin. The perception ond drawing obility of the mon with the lesion were intoct, but his color perception wos completely gone. He wos much more profoundly colorblind thon the red/green colorblind potient.



the incurable disease of writing

A neurologist reflects on the compulsions and frustrations of literary creativity

interview by PAULA BYRON

IN 1998, A MONTH AFTER COMPLETING HER RESIDENCY, ALICE FLAHERTY '94 gave premature birth to twin boys. One baby did not survive the complicated delivery and the other died soon after, clutching his mother with a hand so tiny it barely encircled her finger. For ten days, Flaherty grieved. But then suddenly, she says, "The sun and the moon switched positions." For the next four months,

When my attention wandered during medical school my head. Then my classmates would get mad because they

in a rare postpartum mania, Flaherty experienced her first episode of hypergraphia—the medical term for an overpowering desire to write. She wrote everywhere, all the time: on her left arm as she gripped the steering wheel of her car, on squares of toilet paper in public bathrooms, on Post-it notes in the middle of the night.

As a neurologist at Massachusetts General Hospital, Flaherty was able to diagnose herself—and to put her symptoms to good use. Within a year she had completed her first book, *The Massachusetts General Hospital Handbook of Neurology*, which has since been translated into three languages. And now in a forthcoming book, *The Midnight Disease: The Drive to Write, Writer's Block, and the Creative Brain* (Houghton Mifflin, 2004), Flaherty explores both hypergraphia and its seeming antithesis, writer's block. The *Bulletin* recently asked her about her personal and professional views on literary creativity.

Bulletin: *How did your first bout with hypergraphia begin?*

Flaherty: One morning, exactly ten days after my babies died, I woke up feeling as if a switch had been thrown and a thousand volts were flowing through me. It was like in *Hamlet*, when "the sheeted dead / Did squeak and gibber in the Roman streets." I was filled with an overwhelming compulsion to write. That's all I was conscious of—I had important ideas that I needed to write down because otherwise I would forget them.

Everyone kept saying, "It's a grief reaction," or "She's depressed." But I liked my sorrow. I was *wallowing* in it—I think that would be the appropriate clinical term. Depressed people don't enjoy being depressed; I vaguely remembered that from medical school. I was full of grief, but I was euphoric too, and I had no intention of getting better, even though there were days that I felt that my brain was going to explode, or that I was like a balloon attached to the earth by a single frayed thread.

So I wrote all the time. In the middle of the night, I'd write on a PalmPilot or on tiny Post-it notes. I would stick the Post-its on the wall, collect them the next morning, then type my scribbles into the computer. My husband, Andy, who was incredibly supportive through all this, told me, "That's when I knew you were sick. The smallest Post-its—why not even the medium-sized ones?" I don't know why—it just *had* to be the tiny ones.

About some of my behavior, I'd think, well, doesn't everybody do that? Many people write on their hands; I just extended that up my arm while driving across the Longfellow Bridge. And everyone will suddenly jot something down—but maybe not on toilet paper in the public bathroom, and not for half an hour.

Bulletin: *And didn't you write on napkins in the cafeteria at Mass General?*

Flaherty: Lots of people write on napkins—that's normal! Physicists do it all the time. Go to MIT. They're all in the cafeterias writing on napkins. Except when they attend fancy dinners—then they write on the damask tablecloths.

Bulletin: *What were you scribbling on all those Post-its and napkins?*

Flaherty: It was largely autobiographical. Some of it was just phrases, ideas that I can't decipher now but at the time led me on all sorts of tangents. It was a mentally ill flight of ideas, and yet those scribbles were where most of the ideas for my book on writing came from. As it is, the book is largely memoir disguised as neurology.

But if I were hypergraphic all the time, I could never be a writer. First of all, I'd die of exhaustion. And the writing would be much too personal and disorganized, its associations too loose. Editing is best done when you're normal or a whiff depressed, willing to toss out the trash.

Then, after four months of mad scribbling, another switch was thrown, and I became completely torpid, with no impulse to write—or even to move. It was peaceful, unless I tried to write or speak. Then I felt as though my lungs were full of water. That lasted about six weeks.

The following year, by a strange symmetry, I gave birth to premature—but healthy—twin girls, my wonderful daughters Katerina and Elizabeth. Again, I experienced four months of hypergraphia followed by a short period of semi-catatonia.

Whatever brain-hormonal interactions caused hypergraphia in me might have caused more traditional postpartum psychosis in someone with a different premorbid personality. The truth is that, even before the pregnancies, I'd always been inclined to write a bit more than normal. When my attention wandered during medical school lectures, for example, I would furiously write whatever thoughts came into my head. Then my classmates would get mad because they assumed I had taken great notes that I just wasn't willing to share. And this past summer I tried hard not to start a new book—the result was an oratorio libretto about Jacob wrestling with the angel, a 165-page biographical sketch, and a children's book on the adventures of a picky eater and the Loch Ness monster.

In general, hypergraphia doesn't guarantee great writing, just lots of it. Hypergraphics tend to be internally driven; they write for their own pleasure or to deal with their own demons. Being paid a dollar a word can make you prolific, but it's not the same as being hypergraphic. Sometimes hypergraphia can take the form of copying the same poem over and over. I've done that, because of the black-

lectures, I would furiously write whatever thoughts came into assumed I had taken great notes that I wasn't willing to share.

WORDS' WORTH: Alice Flaherty, who has experienced firsthand the hypergraphia she now treats in patients, considers the phenomenon both a disease and a blessing.

ness of the letters on the page and the way the vowels rang like bells in my head. Or hypergraphics make useless lists of everything, like lists of their favorite songs. And to a more pathological extreme—I can't think of a tactful word—

Bulletin: *Like Jack Nicholson in* The Shining?

Flaherty: Yes, typing reams of "All work and no play makes Jack a dull boy."

Bulletin: *Which famous authors have been hypergraphic?*

Flaherty: Isaac Asimov, who wrote nearly 500 books, is a classic example. He would sit down and compose 90 words a minute on his typewriter and reportedly never suffered a blocked moment. Everyone thinks of Proust as hypergraphic because he wrote such a long novel over such an extended time. Other writers often described as hypergraphic include Stephen King, Charles Dickens, Honoré de Balzac, Agatha Christie, Anthony Trollope, John Updike, Herman Melville, and Joyce Carol Oates.

Bulletin: *You mention in your book that Joyce Carol Oates objects to people calling her writing compulsive.*

Flaherty: Yes, and I can understand that, since most people consider "compulsive" an insult. But doctors get blasé about using medical terms. We medicalize everything. When conferences get dull, we entertain ourselves by diagnosing each other—congenital toe walking, swan-neck deformity, frontal release signs.

People don't realize that not all aspects of mental illnesses are terrible, although most mental illnesses, of course, cause great suffering. Some of my patients have told me that, for them, a single episode of depression was far worse than living through World War II or cancer. But an obsessive-compulsive personality can be useful if you're an engineer checking the *Challenger* for flaws. That's going to be my next book: *Make Your Mental Illness Work for You.* If you have narcissistic personality disorder, become a dictator.

I think one reason Joyce Carol Oates gets irritated about being called compulsive is that she derives pleasure from her writing. That's important to remember. Some people write because they're unhappy, but when they're writing, they're often filled with joy.

People who didn't know me when I was hypergraphic ask why I call it a disease, especially since I also consider it a blessing. I call it a disease, in part, because of the way my writing sucked me away from everything else. And because of how strange it felt to be suddenly propelled into a creative state by what were probably postpartum biochemical changes. I hated to think that writing—one of the most refined, even transcendent talents—should be so influenced by biology. On the other hand, as a neuroscientist, I realized that if we can get a handle on fluctuations in creativity, we might be able to find ways to enhance it.

Bulletin: *What causes hypergraphia?*

Flaherty: Certain brain conditions can trigger it, and they all seem to involve the temporal lobes. It was Norman Geschwind ['51] and colleagues who first showed an association between temporal lobe epilepsy and hypergraphia. Fyodor

One of my patients was referred to me because a drug her pocketbook and on her clothes. She even wrote ten-page

Dostoevsky's temporal lobe epilepsy almost certainly caused his prolific writing. Just before his seizures, he would enter a state of religious ecstasy in which his world was flooded with meaning. Between seizures, he wrote hypergraphically, often about his struggle with the fact that the periods in which he seemed to experience the highest truths were also the product of a disease.

Like Dostoevsky, some people with temporal lobe epilepsy display a group of personality traits—collectively called the Geschwind syndrome—that include hypergraphia, strong religious or philosophical interests, and wild mood swings. But about 50 years before Geschwind did his work, the German psychiatrist Emil Kraepelin described hypergraphia in people with bipolar depression.

Although at first glance temporal lobe epilepsy and bipolar disorder seem quite different—one a neurological disease with seizures, the other a psychiatric disorder with mood swings—on closer examination, the symptoms and the treatment overlap a great deal. Clinicians often have trouble deciding whether to diagnose temporal lobe epilepsy or bipolar depression in patients today, so imagine how difficult it is to identify the afflictions of people long dead. Biographers have diagnosed Edgar Allan Poe and Lord Byron both ways as they have tried to account for Poe's and Byron's prolific writing and mercurial temperaments.

Schizophrenia also can cause hypergraphia. With his copious manifestos and journals, Theodore Kacyznski, the Unabomber, is a classic example of a high-functioning schizophrenic who became hypergraphic. Drugs sometimes induce hypergraphia as well. One of my patients was referred to me because a neuroleptic her doctor had prescribed suddenly made her start writing in her pocketbook and on her clothes. She even wrote ten-page letters to her parents while sitting in the same room with them. And Robert Louis Stevenson churned out all 60,000 words of *The Strange Case of Dr. Jekyll and Mr. Hyde* during a six-day cocaine high.

Bulletin: *Don't a high proportion of writers have bipolar disorder?*

Flaherty: Yes, or depression with bipolar features. The work of psychologist Kay Redfield Jamison and others has shown that writers are ten times more likely to be bipolar than the rest of the population, and poets are a remarkable forty times more likely.

Bipolar disorder is strongly genetic. You can see this in writing families like the Jameses, in which the mildly affected members are more productive than both their relatives with a more severe form of the disease and the general population. Henry James had unipolar depression and his famous siblings William [Class of 1869] and Alice were mildly bipolar, but their brother Robert's writing career was crippled by his severe bipolar disorder.

Danielle Steel, whose late son also had severe bipolar disease, likely has enough of the bipolar gene cluster to make her hypergraphic—she's published more than 60 books—but not enough to be impaired. Severe mental illness leaves little room for creativity. Sylvia Plath, who was bipolar, once said, "When I was ill, that's all I was."

Bulletin: *In your book, you state, "Hypergraphia is neither painful (except sometimes to the reader) nor common. Writer's block is both."*

Flaherty: Yes—all blocked writers share two traits: they don't write despite being intellectually capable of doing so, and they suffer because they're not writing. One of my favorite descriptions of block was by a nineteenth-century English poet, John Clare: "They have cut off my head, and picked out all the letters of the

her doctor had prescribed suddenly made her start writing in letters to her parents while sitting in the same room with them.

alphabet—all the vowels and consonants—and brought them out through my ears; and then they want me to write poetry! I can't do it."

The list of famous writers with block is long—Franz Kafka, Virginia Woolf, Saul Bellow, William Styron, Sylvia Plath, Norman Mailer, Ralph Ellison, Katharine Mansfield. Gustave Flaubert, who had temporal lobe epilepsy and wrote hypergraphically, crossed out nearly as many words as he wrote. Of course, these writers managed to be productive enough to become famous. One of the tragedies of block is that it also afflicts unknown people—talented individuals who just disappear from their fields because they stop being able to produce. That's why treating block as a disease isn't frivolous.

Bulletin: *Is writer's block the true opposite of hypergraphia?*

Flaherty: No. Originally I thought it was, but you can suffer from both almost simultaneously, whether they alternate at different times of year—as in people with seasonal patterns of productivity—or whether you're blocked in one genre but not in another. Samuel Taylor Coleridge is a classic example of this: he used to churn out metaphysical treatises at the same time that he was paralyzed in his attempts to write poetry, which is what really mattered to him.

So, from that phenomenological point of view, hypergraphia and block seem too closely related to be considered true opposites, just as mania and depression are difficult to present as complete opposites. Everyone from Freud on has argued that mania is, in many ways, closer to depression than it is to the normal emotional state. And that's true on a number of axes, including treatment. Treating the mania often treats the depression.

There seems to be a frontal/temporal lobe interaction that is important for writing—and probably other creative endeavors—and if this interaction becomes imbalanced, problems arise. In people with injuries to the temporal lobe, you see disinhibitions and loquacious speech, as opposed to the laconic kind of speech typical of frontal lobe injuries. Wernicke's aphasia, where you talk gibberish, and Broca's aphasia, where you struggle to speak, are the classic examples. And there is evidence, although preliminary, that when your frontal judgment mechanism gets out of control, you can end up with creative block.

The frontal/temporal lobe axis turns the received view of creativity 90 degrees, because until recently, the only theories about the creative brain were ones that speculated that the right hemisphere is the seat of creativity and the left hemisphere just helps you do your taxes. I'm oversimplifying, but the picture is still much more complicated than even the best of those theories suggest—not only because of the way the temporal lobes on both sides may drive creative work, but also because of the role the frontal lobe may play in judging or editing the often over exuberant products of temporal lobe changes.

Bulletin: *How can writing disorders be treated?*

Flaherty: For many hypergraphics, the question should be, do they want to be treated? And what exactly is it that you're treating? Is it bad hypergraphia, in that they write poorly? Or are you treating hypergraphia in which the quality of writing is relatively good, but they're so obsessed with writing that they're alienating family and friends?

For hypergraphics who want help, redirecting some of their energy to the editing phase can help. And mood stabilizers are both anticonvulsants and antimanics, so they get at the two most common neurological causes of hypergraphia, temporal lobe epilepsy and mania.

As for block, writers have a long history of self-medicating, usually unsuccessfully, with everything from alcohol to coffee to amphetamines. These days, people who complain to a psychiatrist of writer's block tend to be treated for depression or anxiety.

Also, some blocked writers struggle with critical inner voices. The writer Anne Lamott personified one of these critics as, "the vinegar-lipped Reader Lady, who says primly, 'Well *that's* not very interesting, is it?'" Low doses of atypical dopamine antagonists may quieten those inner voices.

Bulletin: *You mention in your book that different parts of the brain control the drive to write and the ability to write. Can you elaborate on that?*

Lucky Stars

Some authors are blessed with a prolific—even compulsive—capacity for writing

Danielle Steel
Stephen King
Marcel Praust
Isaac Asimov
Honaré de Balzac
Joyce Carol Oates
Henry James
Edgar Allan Poe

Doctors who write have a rich experience to mine. scientific papers and case workups in a prose style that is

Flaherty: Roughly, the limbic system primarily controls emotion and drive and the cerebral cortex is more concerned with cognition. Yet the neurology of emotion and cognition are tightly intertwined. The cortical area that is the most connected to the limbic system is probably the temporal lobe. And the reason the temporal lobe can trigger hypergraphia is probably because the limbic system produces our strong biologic drive to communicate, which in turn drives the speech area of the temporal lobe.

In psychological terms, it seems that drive is more important than talent in producing creative work. The psychologist Dean Simonton has argued, for example, that the composers who produced the greatest music were simply the ones who wrote the most. Mozart and Beethoven composed all the time, whether walking down a street or attending a dinner party.

Bulletin: *What can writing disorders teach us about creativity?*

Flaherty: Temporal lobe changes can increase creative drive in fields besides writing; for instance, one kind of temporal lobe dementia causes people to begin painting or composing even though other aspects of their lives are degenerating. Vincent van Gogh—who almost certainly had temporal lobe epilepsy—painted with an amazing fury, sometimes producing a fresh canvas every 36 hours. At the same time, he wrote several long letters a day to his brother, Theo. Robert Schumann, who had bipolar disorder, wrote feverishly at the same time that he was composing music feverishly.

The rate of mental illness is about 70 percent for musical performers, poets, prose writers, painters, and composers, but only 25 percent for doctors, scientists, politicians, and businesspeople. Does that mean that doctors' creativity stems from a different source? Or that they are less creative? I'd guess it's that doctors have more social pressure to hide psychiatric illness. After all, physicians have higher-than-average suicide rates.

Clearly, though, you don't have to be sick to be creative. It may be that engaging in creative work not only is a sign of health, but also makes you healthy. The relationship between illness and creativity doesn't mean we should foster disease. Perhaps we should think of creativity as an adaptive response to difficult situations such as illness. Many plants won't bother to flower unless they're stressed just a little; people are like cyclamen.

Focusing on the relationship between illness and creativity is also useful because mental illnesses are often exaggerations of normal brain states that allow us to see more clearly how a mechanism works, even in healthy people. It would be tragic to go from there to pathologizing creativity, though. It makes more sense to go in the opposite direction and notice that everyone shares traits with the mentally ill. Unfortunately, doctors are trained to see all facets of illness as bad, and we tend to dismiss patients who complain of "soft" medication side effects, such as decreased creativity, as simply being noncompliant.

Bulletin: *Why are so many doctors also writers?*

Flaherty: Just the other night, I was sitting next to a department chairman at a stuffy dinner party. He was asking questions about my book, and I began to suspect that his interest was more than casual. So I asked him pointblank, "You write, don't you?" "How did you know?" he replied, sounding defensive. I pursued it: "What are you working on?" He hemmed and hawed, and I finally interrupted, "You're writing a thriller, aren't you?" Of course he was—they all write thrillers. I could name you ten Harvard doctors who are writing thrillers. At least the young ones are; when they get older, they write memoirs.

Doctors who write have a rich experience to mine because they're constantly confronted with issues of life-and-death importance. It's that limbic tug—the ache and blood of medicine.

The flip side of that, though, is that doctors are trained to write scientific papers and case workups in a prose style that is not only bad writing, but also often actively neurotoxic to creativity. I'd bet if you did volumetric MRIs of residents exposed to the typical progress note, with its passive voice and its refusal to describe the patient as a human being rather than as a collection of prostheses and malfunctioning organs, you'd find that after four years the language areas

PHOTO: BETTMANN/C. RBIS

Les Misérables

Many famous authors have wrestled with the torments of writer's block

Franz Kafka
Virginia Woolf
Saul Bellow
William Styron
Sylvia Plath
Ralph Ellison
Mary McCarthy
Norman Mailer

The flip side of that, though, is that doctors are trained to write not only bad writing, but also often neurotoxic to creativity.

of the residents' brains had shriveled up to the size of walnuts. Just a suspicion.

Bulletin: *You seem to be focusing your own research more and more on issues of creativity. What are you working on now?*

Flaherty: I'm interested in biological interventions that affect creativity. For instance, my colleague Shelley Carson and I are studying the effect of lightboxes on undergraduates, because even people without seasonal affective disorder seem to experience winter dips in productivity that could benefit from phototherapy.

As for drugs, I'm primarily interested in those that affect dopamine. Many creative people with mood disorders hesitate to take dopamine antagonists—the neuroleptics—because they feel that the drugs flatten their creativity. If we could show that the newer neuroleptics don't dampen creativity, compliance might improve. That would be incredibly beneficial, especially for people at high risk for suicide.

Another study will focus on stimulants like Dexedrine, because a fair number of studies suggest that stimulants can actually boost creativity. But they need to be used only intermittently and in low doses—sometimes a difficult proposition, given their addictive potential.

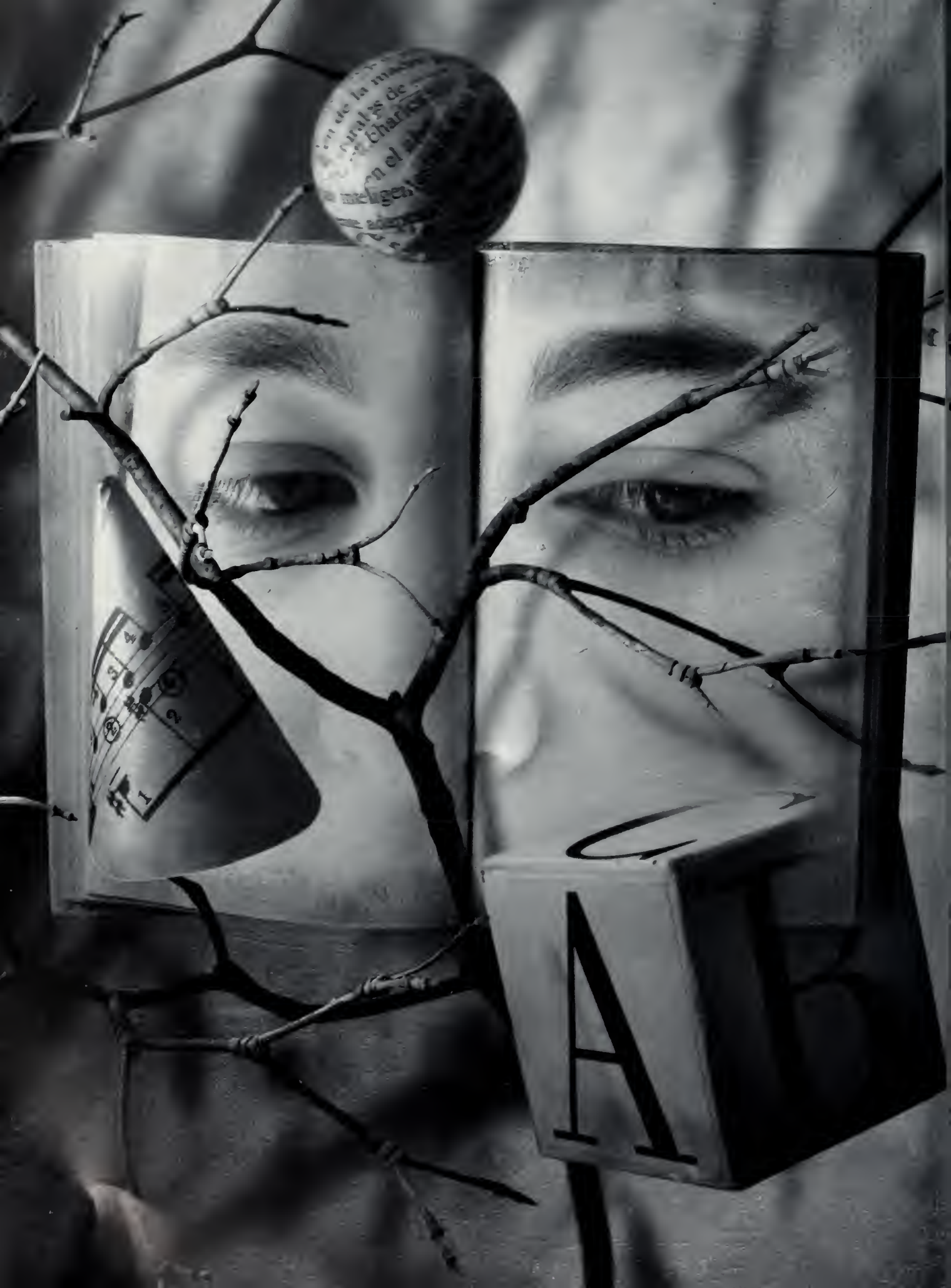
Much of my research has been on the basal ganglia's role in initiating movement, and I have been intrigued with their role in sparking ideas as well. Some patients who have deep-brain stimulators for movement disorders like Parkinson's disease experience profound changes in mood and idea generation.

One of my patients, who has Tourette's syndrome, is a remarkable example of this. Although her tics have nearly disabled her—she has broken her limbs and blinded one eye, she works successfully as a medical editor, is happily married, and is so bright and persuasive that two of my colleagues at Mass General—Emad Eskandar and Rees Cosgrove—agreed to her request for experimental surgery to preserve her remaining vision. The stimulator has helped calm her tics—I no longer hear her chirps and cusses down the hall. To our surprise, though, it also controls her moods and her creativity.

When her stimulator releases current deep under her frontal cortex, she gets mildly depressed and has little interest in getting out of bed, likely because the stimulator has inhibited her nucleus accumbens, a dopamine-rich region of the brain involved in drive. But when we stimulate less deep in the brain, which probably activates her nucleus accumbens, she stops sleeping and begins sending me long emails with all kinds of grand schemes—biotech companies, new government agencies. Because she's so smart, though, they're not just crazy ideas, but *good* crazy ideas. Our next step will be to test her on various creativity parameters with the stimulator turned off, then back on.

Less invasive technologies, such as transcranial magnetic stimulation, may offer some of the same effect temporarily. One case report even described a subject in whom TMS had induced the sensation of being visited by the Muse.

It may seem ludicrous to imagine sitting under a contraption resembling an old-fashioned hair dryer to stimulate your creativity, like something out a 1950s sci-fi flick. But it's not just a question of ridding writers of their block because of publish or-perish pressures. There are worldwide problems urgently in need of creative solutions. Just imagine if you were trying to develop a vaccine for a lethal new virus and a wand waved over your temporal lobe could help you. To the extent that insights into the writing process may carry over into broader problem-solving realms, they have the potential to benefit many people in profound ways. ■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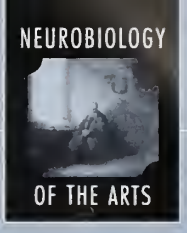


the defiant muse

A patient turns to poetry to try to preserve the memories he is fast losing to disease

by RAFAEL CAMPO

EDUARDO STARTED SPEAKING TO me in English as I welcomed him into my exam room that late spring day, which was odd because we'd always conducted our discussions in Spanish at his semiannual visits. I noticed his English was halting and too formal, like the way my grandparents had spoken it; I assumed he had learned his second language relatively later in life, as they had. This linguistic rigidity would soon prove portentous. ▪ Eduardo was 76 years old and, except for mild hypertension and diabetes, was remarkably well preserved. He wore his thick black hair combed back with a strong-

Eduardo began to create poems that seemed to b
He wrote a poem about what he liked to buy at the supermarke

smelling pomade, and in his suit jacket's pocket a handkerchief folded as precisely as an origami figure declared his fastidiousness. He told me that he had once been a promising young writer in his native Ecuador, but unmentionable circumstances had forced him to leave the country. When he arrived in America he could only find work as a bellhop at an upscale hotel. He had stayed in that job for 40 years; it had been backbreaking work, leaving precious little time, he always said, for cultivating one's mind. Now that he had finally retired, he vowed that would change.

"Eduardo," I said to him in Spanish, "it's Dr. Campo, remember? We can talk in *castellano*." I expected the flash of his smile, the perfect white teeth that I had learned were actually dentures when, to my surprise, he had popped them out into his cupped palm in a smooth, single-handed motion the day I first examined him; instead he stared at me vaguely, as though I were speaking in tongues.

I didn't make anything then of the faint tremor in his right arm. In another moment or two, he became his usual loquacious self again, telling me all about his beloved granddaughter's recent piano recital. Out of his wallet came the latest picture of her, her pigtails tied in pink ribbons, her smile as brilliant as his, the flash of the camera reflected in one side of the shiny black piano against which she stood. He then segued to his grand plans to tour Spain, where he would visit the haunts of Federico García Lorca, Salvador Dalí, and other members of the avant-garde who had been the heroes of his youth. After a check of his blood pressure and a few marks on a lab requisition, I sent him on his way.

In the ensuing few months, I diagnosed Eduardo with Parkinson's disease, which progressed so rapidly that he never made his trip to Spain. He fell in his apartment while preparing his supper a few weeks later; he was unable to take the pot off the stove, and the burning *arroz con pollo* was what may have saved his life, by setting off the fire alarms in the building. The paramedics found him prostrate beneath the table in his kitchen, his left hip broken, his neck bleeding, gashed where the knife he'd been using happened to strike him as he crumpled to the floor. As they wheeled him out on a stretcher, he must have asked them to bring along his writing materials; perhaps he had been in the middle of composing a poem, taking a fateful break to slice some tomato for his salad while the rice simmered.

He had pen in hand when I strode in to see him in the hospital the morning after the accident. Now I recognized that the blank stare was not so much disorientation as one of the subtler signs of Parkinson's disease, which robs those it afflicts of most facial expression. A fat wad of gauze was taped to his neck. "Do you like my new friend?" he asked, referring to it with a downward motion of his chin. "It's like a second head, only it has no brain." With that, he mustered a broad smile, displaying his fine false teeth. But it soon vanished again.

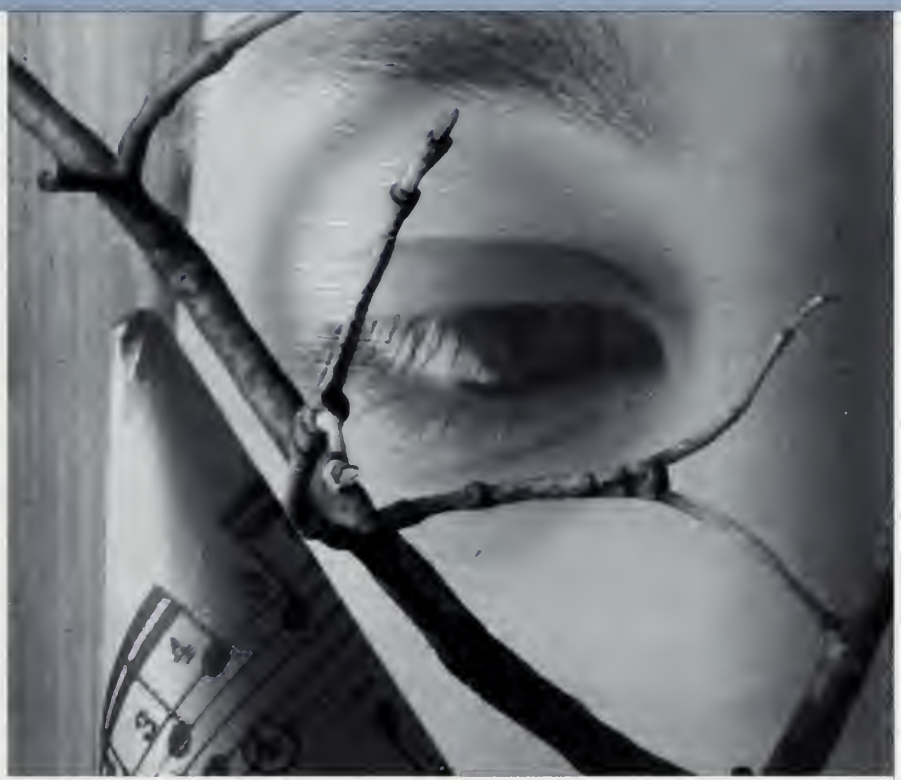
When he left the hospital for rehab, after a taxing two weeks of surgery complicated by post-op pneumonia, he presented me with a small packet of poems. They were difficult for me to decipher, line after line of tiny, shaky cursive in Spanish. Because the ink was blotched and uneven, I guessed he had used a fountain pen to write them. It was the first time he had ever shared his work with me, prompted, surely, by his sudden clash with infirmity.

He asked me what I thought of his poetry when he returned to see me in the clinic. I was not especially inclined toward literary critique that day; he'd weathered a prolonged rehabilitation that had been hampered by a further steep decline in his neurological condition, and we had much new information to review. By now, almost four months later, his gait had become a slow shuffle; his head CT showed the possibility of multiple small basal ganglia infarcts that the neurologist thought might explain his dramatic deterioration. His forgetfulness had also worsened, to the point where when I asked about his granddaughter, whether she had played any new pieces for him, he couldn't remember that he even had a granddaughter.

Yet the poems, those he could remember. In fact, he told me he had set himself the task of memorizing them, to combat what he called "the stealing of my personhood." I wasn't sure whether he meant the disease itself, or the sedatives that were used to calm his agitation in the evenings—a common phenomenon called "sundowning" in medicalese (and a good if rare example of a medical term for something awful that tries to make it sound somewhat poetic).

I sat dumbfounded as he went on to recite about a hundred lines of his verse, the tears coming to his eyes as he described, in one particularly moving section, his granddaughter at the piano, the same talented little girl whom he hadn't been able to recall earlier during our visit. His words rose and fell with all the musicality of a Beethoven or Bach concerto, as if her inerasable pres-

attempts to graft himself back onto the life he had once known. another recorded the names of the streets in his neighborhood.



ence in his mind had found a last remaining outlet. I wondered whether he had indeed once published his work, in the homeland he could no longer name, in a world that he was fast losing.

Eduardo began to create poems that seemed to be attempts to graft himself back onto the life he had once known. He showed them to me when he came to his appointments, now accompanied by his new attendant, a jovial, buxom, copper-haired Haitian woman named Antoinette. He wrote a poem about what he liked to buy at the supermarket; another recorded the names of the streets in his neighborhood; still another, the names and relationships to him of various family members. There was even a love poem for Antoinette, which made her blush when he read it aloud, though I was quite sure she didn't understand Spanish. I was struck by how the language of his poems flowed so effortlessly, no matter how mundane their subjects, animating his face again with the emotions he otherwise could no longer manifest. I noticed how they recollected information, much of it practically useful, some of it simply pleasing, that his faulty neurons could no longer store.

A few more months passed; another springtime in Boston arrived, the golden daffodils like trumpeters heralding a dainty queen's imminent visit. Eduardo failed to keep his morning appointment one day; the inevitable phone call came the same afternoon, from Antoinette. "Don Eduardo, he die," she reported tearfully. She said she had found him utterly motionless in his bed when she'd come to bring him for his appointment; she had recognized immediately that the stiffness in his limbs when she tried to rouse him was very different from that caused by Parkinson's disease—"No medicine help him now," is how she put it. I thanked her for taking such good care of him. After a moment of silence, she told me that she had found something he had left in his apartment for me and that she would bring it to the clinic the next day.

What she brought was a beautifully handmade book of his poems. Pasted on the cardboard cover was an old photograph of a handsome man with thick black hair combed back neatly. His expression was either very serious or a little scared. He sat at a small desk, upon which were assembled some sheets of paper, a stack of books, and a fountain pen with its inkwell; he had cocked his head, as though his concentration had just been interrupted. The desk was positioned before a window, through which I thought I could make out a view of distant mountains, and at their feet, a rim of beach and black water. "*Poesía*" was inscribed in a familiar, tremulous hand beneath the photograph.

Later that week, at his funeral, I sat in a pew alone at the back of the church. After the service, I gave the book to a little girl in pigtails, who smiled at me so genuinely I felt as though I'd known her all her life. ■

Rafael Campo '92 practices medicine at Beth Israel Deaconess Medical Center. This essay was reprinted from his most recent book, The Healing Art: A Doctor's Black Bag of Poetry,

PHOTOS: JESSIN DE LIRAMO AND LOUISE WHEATLEY/PHOTONICA

the sound

In unraveling the puzzle of how music affects the human brain, neurologist

Mark Jude Tramo

WHEN THE BEATLES INVADED HIS HOMETOWN TO MAKE THEIR debut on the "Ed Sullivan Show," seven-year-old Mark Jude Tramo found himself captivated. By then, his own precocious musical abilities had caught the eye of a talent scout. At the 1964–65 World's Fair, Tramo played classic rock 'n' roll on electric guitar for the crowds. By nine, he was performing as a folk guitarist at Catholic churches. In high school he was writing songs. And he produced his first musical show—a rock musical—at seventeen.

While earning his undergraduate and medical degrees, Tramo played in a rock group whose demo landed him and his bandmates a coveted audition at RCA Records. But RCA's offer arrived the same week that Tramo matched

# of music

may help broaden music's healing potential *by* BEVERLY BALLARO

in neurology at his first-choice hospital. "Given the vagaries of making it in the music industry," says Tramo, "the choice was clear, but heart-wrenching."

The recording industry's loss became the medical profession's gain. When Tramo saw that a new science, dedicated to understanding music perception and cognition, was on the horizon, he seized an opportunity to combine two passions. During his residency, it occurred to him that the new digital technologies he was using to record music could facilitate neuroscientific studies of musical timbre recognition. And he realized that research into how humans perceive music could potentially contribute to new therapies in the realms of deafness, stroke rehabilitation, and palliative care.

To unlock the puzzle of how the brain processes tonal information, Tramo began working with stroke and split-brain patients. By analyzing which music-processing functions these people were unable to perform, he helped determine which regions of the brain are involved in certain music-related activities. Those studies inspired Tramo, with colleagues in the Harvard Program in Neuroscience, to develop an experimental model for the neural coding of pitch and harmony in the auditory cortex of primates.

The clinical applications that may one day arise out of such understanding are the driving force behind Harvard's Institute for Music and Brain Science, which Tramo co-founded in 2002. The institute is dedicated to advancing knowledge about the neurobiological foundations of music and fighting diseases that impair the capacity to perceive, learn, and perform music. Its research also focuses on using music to treat children and adults with neurological and other diseases.

Music therapy, says Tramo, may benefit patients in every phase of life, beginning with premature infants. "Babies in neonatal ICUs are isolated in incubators," he says. "They can't see well and are subjected to an acoustically stressful environment because of all the monitor alarms going off." Some studies suggest, he adds, that music can help premature infants gain weight faster, avoid cardiopulmonary distress, and leave the ICU sooner.

"The degree of neonatal music sensitivity is amazing," says Tramo. "Babies can perceive sounds in the womb beginning at about the midpoint between conception and birth. By four months of age, they will respond to dissonant chords in music by squirming and turning away from the source." Research, he adds, indicates that musical preferences are determined in part by environmental exposure. "It's analogous to the way humans are born with a capacity for speech," he explains. "Children quickly learn the 'language' of music for their particular culture."

Yet infants also display preferences for certain musical features that cut across cultural boundaries. Whether based on seven notes, as in most Western music, or five notes, as in some Eastern traditions, Tramo adds, the music of

"By four months of age, babies will respond to dissonant

all cultures relies on an octave structure that can be broken down into a limited subset of pitches that are consistent from one octave to the next. Babies have the auditory capacity to recognize octave similarity.

Infants are not the only potential beneficiaries of scientific insight into the way the brain responds to music, says Tramo. Tonal information processing studies may one day lead to applications in speech therapy and the treatment of dyslexia in older children. Adults, too, may benefit from mood induction therapy—the use of music to deal with chronic pain or to reduce the discomfort, anxiety, and depression that often accompany diseases such as cancer.

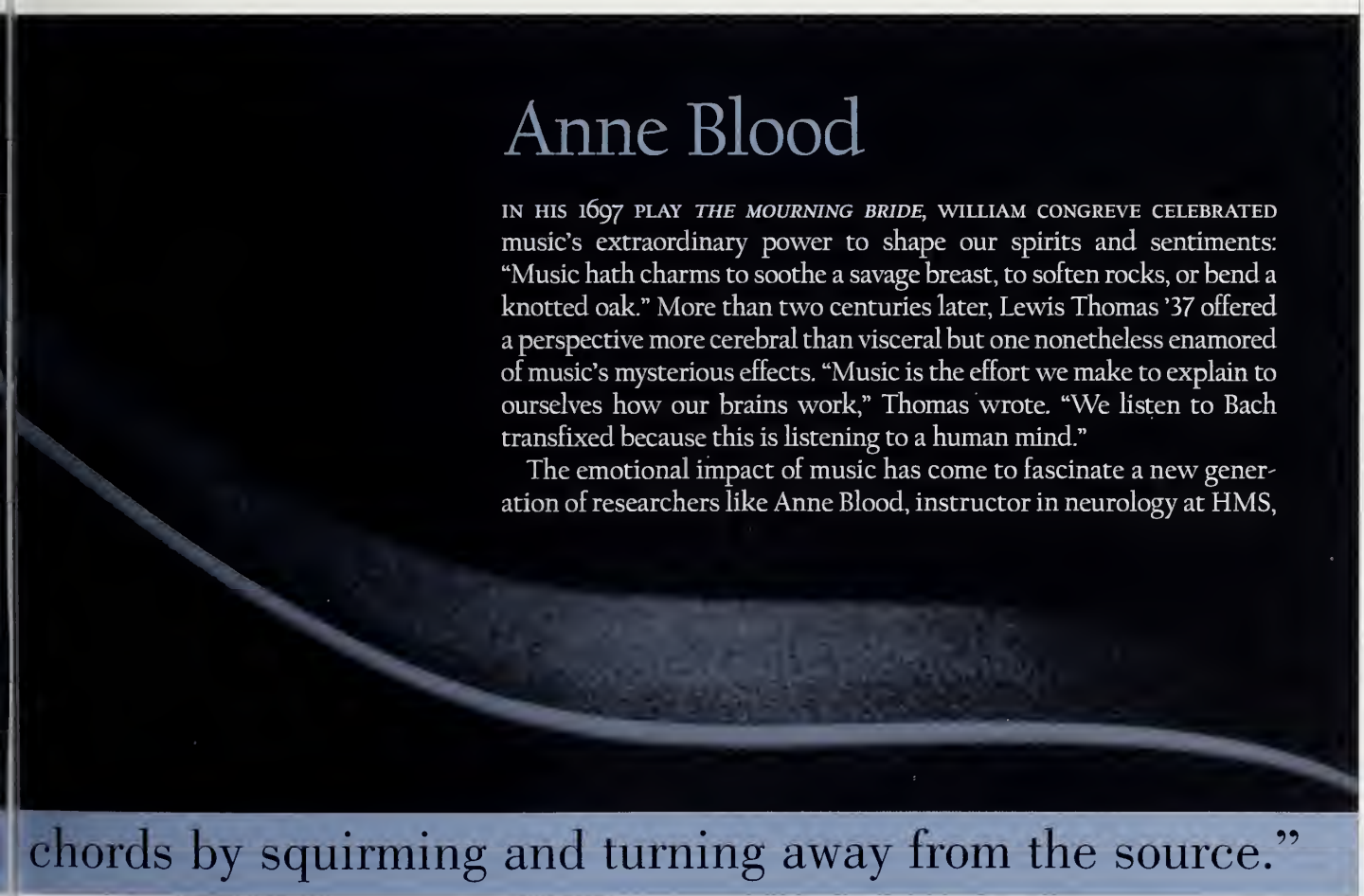
Some studies have suggested that exposure to music can modify the widely fluctuating blood pressure that many coronary bypass patients experience postoperatively. Other studies indicate that music can help calm aggressive behavior, a common problem with Alzheimer's patients. And understanding how the ear and the brain process music can lead to the development of better hearing prostheses, cochlear implants, and other bionic devices that may alleviate deafness.

Although music therapy is already being used to help patients, Tramo acknowledges that "many of the data still fall into the realm of the anecdotal." The lack of rigorous, controlled clinical studies has prevented music therapy from achieving the status of a treatment whose value is officially recognized within the medical profession and covered by insurance companies.

Tramo believes that the effects are there for the measuring. "We already understand much about how different parts of the brain 'talk' to each other," he says. "We know, for example, that the relationship between sounds and emotions has an anatomical basis. The nerve cells in the auditory cortex connect to the nerve cells in the medial temporal cortex, which controls memory and emotions. Those nerve cells, in turn, connect to other parts of the brain that regulate heart rate, blood pressure, and immune response. So, a broad connectivity is at work."

Amid his quest to bring clarity to these kinds of scientific issues, Tramo has not completely forsaken his artistic vocation—some of his recordings are getting airplay on a 1970s rock radio show, and a record label has expressed interest in re-releasing an album he recorded years ago. He is now working on a digital remastering of the material.

But Tramo is devoting most of his energy over the next few years to developing The Institute for Music and Brain Science, studying music perception in stroke and epilepsy patients, and, with colleagues, "cracking the neural code for pitch and harmony" in the primate auditory cortex. And he is writing a book about music, medicine, and neuroscience. "At this point," he laughs, "I think it's safe to say that my rock 'n' roll days are over." ■



Anne Blood

IN HIS 1697 PLAY *THE MOURNING BRIDE,* WILLIAM CONGREVE CELEBRATED music's extraordinary power to shape our spirits and sentiments: "Music hath charms to soothe a savage breast, to soften rocks, or bend a knotted oak." More than two centuries later, Lewis Thomas '37 offered a perspective more cerebral than visceral but one nonetheless enamored of music's mysterious effects. "Music is the effort we make to explain to ourselves how our brains work," Thomas wrote. "We listen to Bach transfixed because this is listening to a human mind."

The emotional impact of music has come to fascinate a new generation of researchers like Anne Blood, instructor in neurology at HMS,

chords by squirming and turning away from the source."

who found herself intrigued by this puzzle while a graduate student living in Los Angeles, the heart of the recording industry. So, while a postdoctoral fellow at McGill University, Blood decided to subject art to the scrutiny of modern scientific tools. With colleagues, she designed and conducted brain imaging studies aimed at illuminating the origins of music's power to sway listeners' moods, both positively and negatively.

To assess which areas of the brain come into play when listeners experience an unpleasant emotional response to music, Blood exposed a group of test subjects to a series of recordings that steadily increased the degree of dissonance. But the first order of business was to ensure that the subjects would, indeed, find the clashing sounds sufficiently unpleasant.

To this end, Blood chose non-musicians as test subjects. She also took care to exclude from the study aficionados of jazz, which characteristically relies on a complex interplay of harmonic tension and resolution.

"It's quite common for trained musicians to develop a taste for dissonance," Blood explains. "The pleasure that many people derive from dissonance is not so much the jarring contrast between two particular notes, but the resolution of that tension into consonance as well as the pleasurable, suspenseful anticipation of that resolution. In the music we used in our study, the dissonance never resolved."

Music historians, in fact, have demonstrated how both the Western definition and perception of harmony have evolved over time. For medieval musicians, harmony consisted of simple two-note combinations. During the Renaissance, three-note chords emerged, and the Romantic Era saw the expansion of chords into four-part harmonies. Modern composers further expanded the meaning of harmony; contemporary listeners now enjoy dissonant chords whose instability would have struck earlier audiences as unbearable. When Blood finally previewed the most dissonant test tape for a colleague, she was gratified by her colleague's assurance that it was so awful, "it nearly made her feel sick to her stomach."

When Blood correlated brain activity with a dissonance level that increased continuously, she made a discovery that contrasted with previous findings. Listening to dissonant sounds did not change activity in the parts of the brain that typically light up in response to other sensory stimuli such as visual cues. Instead, as the music increased in unpleasantness, an area on the right side of the brain indicated by other studies to be important to memory and anxiety—the parahippocampal gyrus—became active.

Blood had more striking findings in store when she recruited a fresh set of test subjects for a study designed to examine the impact of positive emotional responses to music. This time, she chose ten trained musicians, knowing that the likelihood of evoking a powerful emotional response to music would be higher for someone with a lifelong passion for the art. Specifically, Blood wanted

Gottfried Schlaug

FOR GOTTFRIED SCHLAUG, ASSOCIATE PROFESSOR OF NEUROLOGY AT HMS, confirming the astonishing human capacity for neuroplasticity means dispelling the notion that the brains of all musically talented people come preprogrammed with an aptitude for music. "I've been happy to discover that, for the most part, musicianship and the chance to excel at playing a musical instrument are not predetermined by heredity," says Schlaug. "To think that musical potential is already limited at birth would be quite depressing for all of us who believe in the enormous potential of the brain to grow and mature based on experiences."

Yet, Schlaug cautions, it would be a mistake to discount completely the role of genes in the expression of certain musical abilities, such as

Contemporary listeners now enjoy dissonant chords whose

to analyze what goes on in the brains of listeners while they are experiencing a powerful emotional reaction indicated by the physiological sensation of getting shivers down the spine.

"The tricky part, of course," says Blood, "is that, while people from various backgrounds and cultures report a euphoric response to music that uniformly involves sensations of tingling and chills, the music that evokes such a response differs from individual to individual." To solve this problem, Blood asked each musician in the study to select his or her own piece of music. Her only stipulation was that the piece had to be purely instrumental, since the brain will inevitably respond to human voices or vocal cues. Her subjects' choices ranged from the mournful strains of a Barber string piece to the lush orchestration of a Rachmaninoff concerto, although Blood points out that other types of music outside the classical genre can also evoke the same response.

An analysis of the results revealed a pattern of brain response quite distinct from what Blood and her colleagues had observed in their study of unpleasant emotional responses to dissonance. The experience of listening to pleasant music, she discovered, did not evoke responses in the parahippocampal gyrus.

Instead, during their positive, spine-tingling experience of feeling moved, Blood's musician subjects all exhibited increased activities in areas such as the ventral striatum, amygdala, and dorsal midbrain areas—regions of the brain associated with motivation and reward. "This was quite striking," Blood says, "because these subcortical parts of the brain are connected with more basic, instinctive impulses and cravings that all animals exhibit. They are mostly reserved for survival-oriented tasks such as eating and reproduction. These are the same neural pathways that typically show a lot of activity in the presence of sexual arousal, for example, or addictive drugs. And yet, clearly, music is not necessary for physical survival or the perpetuation of the species."

Researchers are still debating why Barber's ethereal *Adagio for Strings* should light up the same region of the brain turned on by earthier drives for food or sex. "Humans are highly evolved," says Blood, "but evolution has left us with a number of primitive emotional systems. It may be that the more evolved parts of our brains somehow patch into the evolutionarily older parts and link to them abstract, higher-level cognitive processes, such as listening to music."

It may take years before scientists arrive, if they ever do, at a definitive answer to the question of why humans have developed such a strong neurobiological basis for the appreciation of music. "Fortunately, the implications of this capacity are not nearly as mysterious," says Blood. "If music can stimulate areas of the brain linked to such intensely positive emotions, this lends scientific weight to the popular intuition that music may offer significant mental and physical health benefits." ■

instability would have struck earlier audiences as unbearable.

absolute pitch. Some families have an increased incidence of this ability—as do 35 percent of Japanese musicians and a roughly similar proportion of Asian American musicians (compared with only 10 to 18 percent of their Caucasian counterparts). Researchers, he says, are still trying to differentiate the impact of early music exposure from potential genetic effects. Age at commencement of musical training is one strong factor in the expression of the absolute pitch phenotype, says Schlaug, adding that other factors may include a particular brain anatomy that is commonly found in musicians with perfect pitch.

But, Schlaug notes, cultural factors may be at work as well. Some researchers suspect that the tonal nature of some Asian languages may lend some of their speakers a more nuanced perception of pitch. Others have pointed to the rigorous early musical education programs that are more common in some Asian countries than in Western nations. "In addition," Schlaug says, "these programs tend to rely on teaching philosophies, such as the Suzuki method, that strongly emphasize learning music through listening rather than through reading notation."

Although the extent to which genes underlie absolute pitch remains a mystery, one conclusion of Schlaug's research is unambiguous: the experience of playing music alters the human brain in profound ways. "The idea that experiences can shape the brain in ways that we can actually measure is relatively new," he says.

This realization came about when Schlaug compared adult musicians with non-musicians. He was seeking any behavioral differences between the two groups, as well as functional and structural brain dissimilarities. He identified not only a number of characteristic differences in the motor and sensory regions of the musicians' brains, but also pronounced changes in the brain regions responsible for translating visual-spatial information into motor commands.

In particular, areas in the superior parietal region and in the lateral inferior temporal region showed significant differences between the two groups. Differences were also seen in the cerebellum, where auditory and motor functions become integrated. The musicians' brains, Schlaug discovered, were bigger in certain, well-delineated brain regions than their non-musical counterparts' brains. Moreover, the degree of difference in the musicians' brains correlated with the intensity and duration of their musical training.

To understand when and how these changes take place, Schlaug and colleagues are conducting a longitudinal study of more than 75 children between the ages of five and seven. The children in the experimental group are taking piano or string instrument lessons; the control group's only exposure to music comes as part of their ordinary school curriculum. The researchers plan to follow the children for at least three years, taking annu-

"The next step is to think about how we can use music to

al brain images and subjecting them to various behavioral and cognitive tests.

Although he has completed only the first year of the study, Schlaug is already seeing, in brain images of the child musicians, differences in the same regions that music transforms in their adult counterparts. He and his colleagues are also tracking any possible transfer effects that instrumental training might have on the children's overall IQs, reasoning abilities, and verbal, visual-spatial, math, motor, and auditory skills.

At first glance, it might seem counterintuitive that a child's ability to bow the violin might also enhance parts of the brain connected to visual-spatial skills. But Schlaug points out that these two realms may be more related than they first appear.

"To play the violin requires the ability to read musical notes," he says, "and then the player's brain has to translate that visual-spatial and time information into specific motor commands. Similar operations might be taking place when someone is assembling a jigsaw puzzle. So, it's easy to see how parts of the brain that are involved in music processing might also become better at other tasks that require a similar processing." Brain-based sharing also takes place between music and language processing tasks, he adds, so that instrumental practice, singing, and rhythmic games may strengthen verbal skills.

"We're learning," says Schlaug, "that the human brain is remarkably plastic and highly responsive to early experiences." At the same time, it is also possible, he notes, that "certain learned behaviors rather than music-specific factors may account for the improved performances of musician children in a variety of realms. In general, musicians learn how to be attentive and disciplined. Their musical training may produce improvements in other areas not so much because of specific brain changes but because it makes them particularly adept at learning how to learn."

Applying this new knowledge to therapeutic opportunities is Schlaug's ultimate goal. "The next step," he says, "is to think about how we can use music to alter the brains of people whose diseases might respond to such changes." To this end, one of Schlaug's postdoctoral fellows, Katie Overy, is testing whether the phonological skills of dyslexic children may respond positively to certain musical components.

Schlaug is also overseeing a study focused on melodic intervention therapy—a way of helping stroke patients with aphasia to regain, through music, the ability to speak. Although singing and speaking do share some brain pathways, Schlaug says, they are sufficiently separate so that these patients can still sing even though they can't talk. "We know the intervention works," Schlaug says, "the question now is to figure out *how* it works and to see where such understanding can help us develop new ways to improve the lives of even more people." ■

Roy Hamilton

THE PHENOMENON OF PERFECT PITCH HAS LONG INTRIGUED SCIENTISTS curious about the interplay of genetics and experience in shaping the human brain. For Roy Hamilton '01, the discovery that blind musicians exhibit absolute pitch at startlingly higher rates than their sighted counterparts came about by two accidents, one cruel and one happy.

The first accident took place some 50 years ago when a number of premature infants received excessive doses of oxygen in their incubators. This exposure caused a displacement of the tissue in their eyes, resulting in the condition known as retrolental fibroplasias, which rendered them totally, permanently blind.

alter the brains of people whose diseases might respond."

ALL THE RIGHT NOTES: A number of well-known blind musicians have perfect pitch, including Ray Charles (pictured here), Stevie Wonder, and José Feliciano.

If people are not exposed to musical training by the age

The second twist of fate occurred while Hamilton, now a neurology resident at the University of Pennsylvania, and colleagues were doing research with 46 of these blind subjects in the Beth Israel Deaconess Medical Center laboratories of HMS faculty members Gottfried Schlaug and Alvaro Pascual-Leone. Hamilton was focusing on the role of cortical plasticity in producing the superior tactile acuity that many blind people display. Yet in the course of interviewing his subjects, he stumbled across claims of perfect pitch by a remarkable number of them. And when Hamilton put his subjects to the test, the results bore out the accuracy of their self-assessments.

Against All Odds

What made the results all the more striking, Hamilton says, is that "the phenomenon of perfect pitch is exceedingly rare." Among the sighted general population, absolute pitch occurs on the order of less than one in 1,500 people. The rarity of this ability may reflect, says Hamilton, what most studies have indicated: that early exposure to musical training seems to be a prerequisite for perfect pitch in most sighted individuals.

If people are not exposed to musical training by the age of 11, they almost never go on to exhibit perfect pitch. By contrast, among musicians who go on to receive Western musical conservatory training, the rate hovers around 18 percent.

To no one's surprise, the nine blind research subjects who reported no musical background did not have absolute pitch. But 12 out of the 21 subjects who had received some musical training—an astonishing 57 percent—did display this talent. And Hamilton was even more intrigued to learn that this startling percentage existed even though the average age at which members of his blind cohort had begun musical training was eight years, four months—much later than the average training onset age of sighted musicians—and some of his subjects were as old as 14 before they first picked up a musical instrument.

"The fact that these blind musicians were still able to develop perfect pitch at two or three times the rate of prevalence among sighted musicians clearly suggests that something unique is going on with blind people," Hamilton says. "The challenge now is to figure out how their brains differ, both functionally and morphologically."

Some Stars Are Born

The idea that the brains of sighted and blind people are not identically wired is not new. It has long been known, for example, that sighted people have great difficulty in mastering Braille. What has not been as clear is how much of the distinction is tied to genetic factors and how much to experiential factors. Absolute pitch, says Hamilton, does appear to have a genetic component.

The chances of perfect pitch existing in identical twins, for example, are higher than they are for non-identical twins. Studies have also confirmed a significantly higher incidence of absolute pitch in certain racial and ethnic groups. Asian populations, for example, seem to have elevated rates of perfect pitch compared with non-Asian populations. And, what's more, these higher rates appear to exist independent of the musical scale or environment in which people from those populations are trained.

In the case of the subjects in Hamilton's study, however, the link between blindness and absolute pitch ability had to be explained in other than genetic terms; all of the subjects in this study had been born sighted but became blind shortly after birth.

Amazing Grace

A clue as to what non-genetic factors might explain the amazing rate of absolute pitch ability in Hamilton's blind subjects came from previous brain-imaging studies comparing sighted musicians with non-musicians. In those studies, researchers had discovered a pattern of anomaly: while some degree of asymmetry normally exists between the left and right hemispheres of the brain in all sighted people—with the left side being larger—this asymmetry is significantly exaggerated in sighted people with perfect pitch.

Yet, in blind musicians graced with absolute pitch, Hamilton says, this characteristic asymmetry doesn't appear as pronounced. "This suggests," he explains, "that if you are blind due to a peripheral cause, such as retrolental fibroplasias, and you've managed to develop absolute pitch ability, the mechanism by which you've done so may differ from that employed by the brains of sighted musicians with absolute pitch."

The leading theory as to what that mechanism might be, Hamilton says, is predicated on the idea of compensation. Some researchers believe that, in blind people, the area of the brain that would normally be used for vision gets co-opted for non-visual tasks, such as music. Functional brain imaging appears to bear this theory out, in that tasks such as sound localization and pitch discrimination seem to increase activity levels in the visual cortex. The dramatically enhanced haptic acuity of such individuals, Hamilton adds, may similarly hinge on a co-opting of the occipital lobe.

"It's really not surprising," Hamilton says, "that this might be the case. Think about it—a whopping 40 percent of the cortex in a normal human brain is devoted to one sense: vision. To lose this particular sense delivers a greater blow than the loss of any other. The brain's remarkable ability to reallocate the sizable assets normally dedicated to sight goes a long way toward enriching the lives of blind people." ■

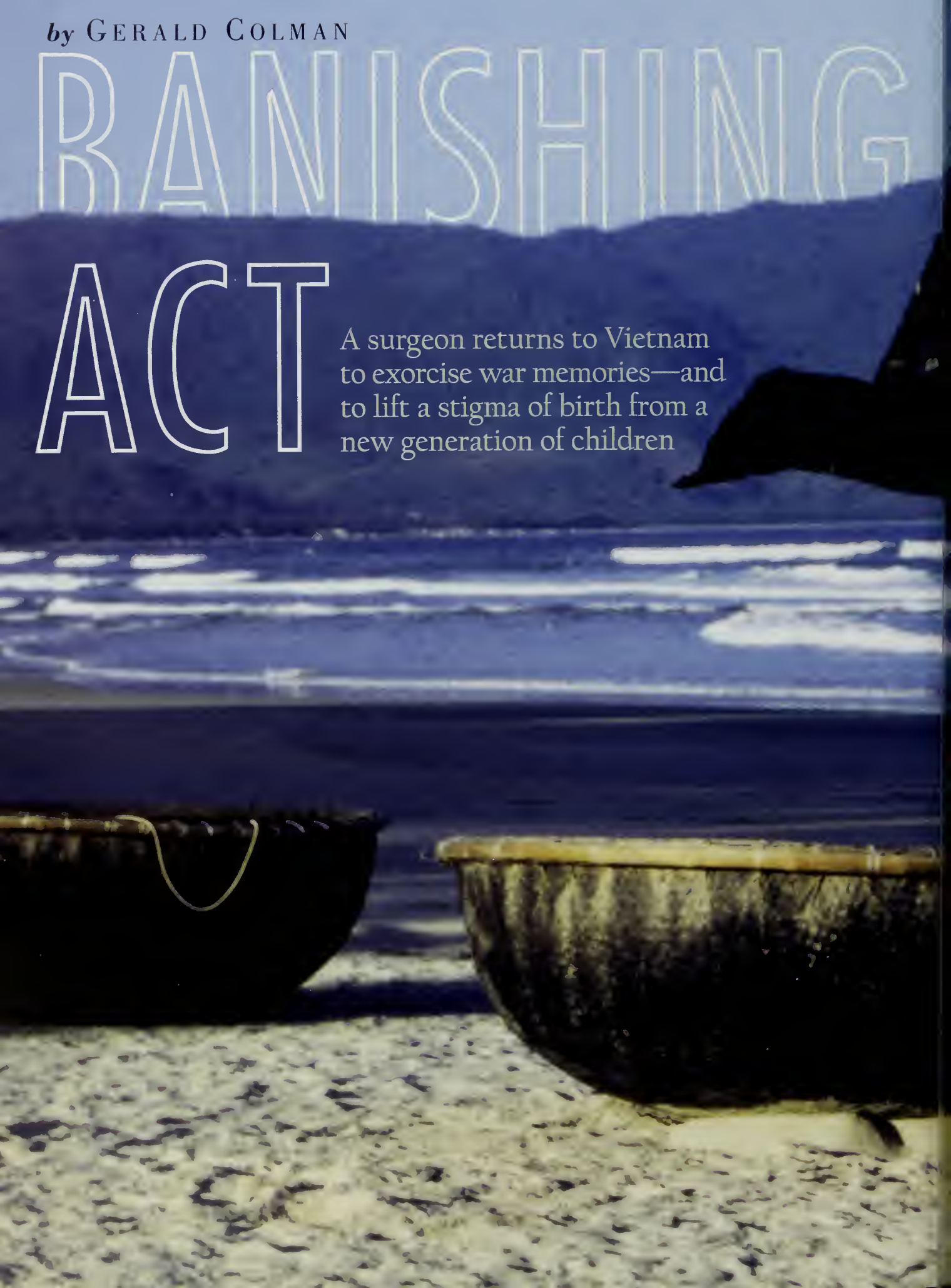
Beverly Ballaro is associate editor of the Harvard Medical Alumni Bulletin.

of 11, they almost never go on to exhibit perfect pitch.

by GERALD COLMAN

BANISHING ACT

A surgeon returns to Vietnam to exorcise war memories—and to lift a stigma of birth from a new generation of children



A DENSE WALL OF STEAM HIT MY FACE AS the heat of the jungle collided with the artificially cooled interior of the plane's cabin. As the other soldiers and I stepped off the commercial jet that had brought me—drafted midway through my surgical residency—to Vietnam in 1969, the stewardesses wished us luck. In the thick jungle air, I could soon hear American F-4 Phantom fighter jets screaming overhead on their way to and from bombing runs in Cambodia. When the pilots cut in the afterburners, the planes would generate a huge, distinctive *kaboom.*

I was initially assigned to a sleepy village along the Mekong Delta. For several days, I almost forgot why I was in Vietnam. I read *War and Peace* and spun fantasies of spending the coming year catching up on all the literature I hadn't had time to enjoy once the rigors of medical school and residency had taken over my life.

Fantasy quickly collided with reality when I was summoned to a meeting with the CIA officer in charge of assigning American physicians to help win over the hearts and minds of the Vietnamese. "You've got surgical skills," he told me, "and they need you bad up in I Corps." My heart sank. Even a novice like me, who'd been in country for only a few days, understood that I'd just pulled the worst possible assignment.

The I Corps area served as a buffer zone in central Vietnam between the forces of the North and South. U.S. and South Vietnamese military units had established bases and outposts all over Quang Tri province and along the demilitarized zone, where the fiercest ground fighting and aerial bombardments of the war were taking place. No one wanted to go there.

Soon after I received my dreaded orders, a clerk came running up to me saying, "Hey Doc, there's a helicopter heading up to Quang Tri that can give you a lift." Two pilots, clad in what appeared to be black pajamas, met me at a Huey chopper. They worked for Air America, a clandestine air carrier that supported the CIA outfit to which I'd been assigned.

On our two hour trip north, the pilots flew low to the ground, hugging the dirt road that served as the main supply artery from the city of Danang to Quang Tri province. We passed over villages, rice paddies, and graveyards, whose traditional round burial mounds were unmistakable from the air.

The helicopter finally touched down in the midst of what appeared to be an old citadel of some kind. "Doc, we're here!" the pilots announced as they dropped me off, in the middle of nowhere. "Have a good tour!" they yelled cheerfully as they took off.

As the whirr of the chopper blades faded, I stood there, dumbfounded, in the middle of a deserted field, clutching a Naugahyde satchel with my tennis racket absurdly sticking up out of it. I couldn't help but panic: had the pilots made a ghastly mistake? My God, had they deposited me on the *wrong* side of the DMZ?

Just as I was ready to jettison all hope, a jeep came into view. The driver introduced himself as an American advisor to the South Vietnamese army, then immediately radioed the local hospital, "Hey, I've got your new doctor!" Exhausted and in a state of shock, I wondered how I would ever survive this godforsaken place for an entire year.

Operational Difficulties

The hospital at Quang Tri was composed of ten buildings located inside a walled compound. It was within those walls that I would quickly find myself, at age 29, a half-trained surgeon charged with caring for a population devastated by its unlucky proximity to one of the hottest military spots on the globe.

By the time the war ended, the heaviest bombing campaign in history had

PHOTOGRAPHY FOR THIS ARTICLE COURTESY OF GERALD COLMAN

destroyed many of the province's villages, and the U.S. military's widespread use of the defoliant Agent Orange had transformed much of the lush jungle landscape into something resembling a lunar surface. But when I arrived, the earth was still green and most of the province's inhabitants had not yet fled. CIA and USAID officials explained that I would be responsible for running a 400-bed hospital designated to serve the needs of all the South Vietnamese civilians and military personnel in the province. If I failed to help these people, they would receive no care at all.

When I learned that I would be delivering all babies and handling all surgery for related complications, my first thought was, "Damn, I haven't done any obstetrics since my student rotation at the Boston Lying-in Hospital." My second thought was that I was going to be awfully busy. I would be solely responsible for 300,000 people, a large percentage of whom were women of childbearing age who gave birth nearly every year.

While working at the hospital, I lived in a compound by the river with two other Americans. Surrounded by a high, concrete wall, our villa was encircled, except for the entrance, by claymore mines. Machine-gun–toting Hmong guards, imported from neighboring Laos, manned outposts on the perimeter.

Although they had been recruited for their fierce anti-Communist sentiments, the guards, clad in ragtag shorts and sandals, had an unnerving habit of falling asleep huddled around their teapot; several times a night we would take turns making sure they were awake. Not long before my arrival, the compound had been violently ransacked by a gang of Vietcong who forced their way in without firing a single shot; they had seized the wife of one of the guards and threatened to kill her before his eyes.

While driving from my villa to the hospital for middle-of-the-night emergencies, I was always fearful of the Vietcong. When a call would come in, I would hop into my jeep and navigate toward the hospital gates. I always kept a loaded M 16 rifle on the seat next to me.

Wet Behind the Ears

On my first day on the job, I encountered a woman with a difficult obstetrical presentation. I knew I had to turn the

IN THE LINE OF FIRE: Previous spread, Chino Beach during a trip the author took in 1993; clockwise from upper left, the author in Vietnam in 1968; the remains of a Catholic church that was destroyed when U.S. forces routed Vietcong who had been hiding there; a wounded Vietnamese civilian on a hospital ship in the South Chino Sea; the hospital in Quang Tri; and the author standing in front of his operating room in 1970

I STOOD THERE, DUMBFOUNDED, IN THE MIDDLE OF THE DESERTED FIELD, CLUTCHING A NAUGAHYDE SATCHEL WITH A TENNIS RACKET STICKING OUT.

baby's head a certain way—I just didn't know *how*. As they exchanged glances, I could sense the doubt of the Vietnamese nurses assisting me.

I announced that I urgently needed to use the men's room. Leaving the patient in stirrups, I retreated to the bathroom, surreptitiously grabbing an obstetrics textbook en route. There, I furiously studied the pictures before returning to the OR and successfully rotating the baby's head, as if I had done it a thousand times. It was my first big surgical test in Vietnam, and I was hugely relieved to have passed it.

More challenges followed. Midwives routinely handled most deliveries but they sent especially difficult cases to the hospital. *Présentation de la poule*—in which the baby's arm was sticking out of the mother's body but his head and body faced backward—was a common complication. So were uterine ruptures. On more than one occasion, I delivered a baby floating free in the mother's abdominal cavity. Once I even found a baby nestled against her mother's liver.

It was not unusual for me to care for a laboring woman who had been transported 30 miles to the hospital on a blanket strung between bamboo poles shouldered by human bearers. One such patient was a woman in labor who had been struck by a guard's stray bullet. The bullet passed through her pregnant belly sideways. When we delivered the baby by emergency C-section, we found that he had sustained a single, small-bore gunshot to his buttock. After closing up the mother, I sutured the baby's wound. Both mother and child made a good recovery.

As time wore on, I grew bolder and more confident, even though my working conditions were unimaginable by the standards of the Boston surgical world. More often than not, flies in the primitive and not terribly sterile OR would alight on the intestines of patients on whom I was operating. Somehow, the patients never seemed to become infected.

The hospital at Quang Tri had no EKG machine, no cardiac monitors, and no x-ray machines except for a relic from World War II. I learned to rely on surgical intuition and common sense. And I learned to improvise. With few sutures available, I found myself using industrial silk to close up wounds. If I bent a needle, instead of discarding it, I bent it back. These habits would later come in handy; when a woman on a plane I was traveling in unexpectedly went into labor, I delivered the baby, then successfully tied off the cord using the string from a tea bag scavenged from the plane's galley.

Tragically, not all of my work in Vietnam revolved around bringing mothers and babies safely through childbirth. I saw many vicious, war-related mutilations. The Vietcong filled landmines with pieces of chain, nails, and other lethal junk

THE HOSPITAL AT QUANG TRI HAD NO EKG MACHINE, NO CARDIAC MONITORS AND NO X-RAY MACHINES EXCEPT FOR A RELIC FROM WORLD WAR II.

SCENES FROM VIETNAM: Clockwise from bottom left, a Vietcong woman wounded in battle whom the author treated for skull fractures; the author and Le Ba Dung performing surgery on a patient with an intestinal wound; the author standing with an M-16 next to a sandbag bunker; food vendors in Hanoi years after the war; Le Ba Dung with two of his children; and the three doctors who ran the hospital at Quang Tri (the author stands in the center)

so that when they were detonated, their contents might blow 30 holes in the intestine of any civilian unfortunate enough to step on such a device. I soon learned to repair such ravaged intestines in four minutes flat.

But first things always came first—after making the initial incision, I often discovered that the patient had an abundance of worms drifting in the abdominal cavity. I would simply scoop the worms out by the handful and toss them into an antique enamel bucket kept at my feet for this very purpose.

Other trauma cases rolled through the OR doors when Vietnamese soldiers carelessly cleared their weapons by discharging them into the air. When the bullets fell back to earth, they sometimes injured unlucky civilians. I once operated on a man who'd been lying on his stomach, asleep in his grass-covered hut, when he was struck by a bullet "falling out of the sky." The round lodged near his spinal column. Although he had arrived crippled by his injury, the patient was able to walk out of the hospital unassisted.

I also saw a heartbreaking number of children. Many of them were burn victims who had sustained horrible injuries from cooking fires that would blaze out of control because Vietnamese mothers had stoked them with military jet fuel. I didn't have a skin-graft knife or mesher available, so I used a straight razor and sterilized wooden shingles as backing to mesh the grafts.

Another large percentage of children I treated were injured by rifle-propelled grenades. Attracted by their fluorescent turquoise color, small children would pick them up and playfully smash them on rocks, causing them to detonate. Other, savvier children knew the risks but cracked open the grenades anyway, hoping to make some money by selling on the black market the abundance of shot found inside.

While about half of my non-obstetrical cases were related to war trauma, the other half consisted of patients suffering from ailments I had previously only read about. Amoebic abscesses and rabies were two of the once exotic, now routine, problems I encountered. I sometimes found huge tapeworms running the entire length of the intestine, and other conditions that, untreated, had simply run out of control; I once removed a 26-pound dermoid cyst, with teeth and hair, from a woman's uterus.

On the flip side, though, I saw almost no obesity in my Vietnamese patients. Surgical training on American patients raised on rich Western diets had accustomed me to expect aortas transformed by disease into thick, arteriosclerotic pipes. It was eye-opening to me to find, in Vietnamese patient after patient, aortas that were thin, pliable arteries beating smoothly with a soft whooshing sound.

Risky Business

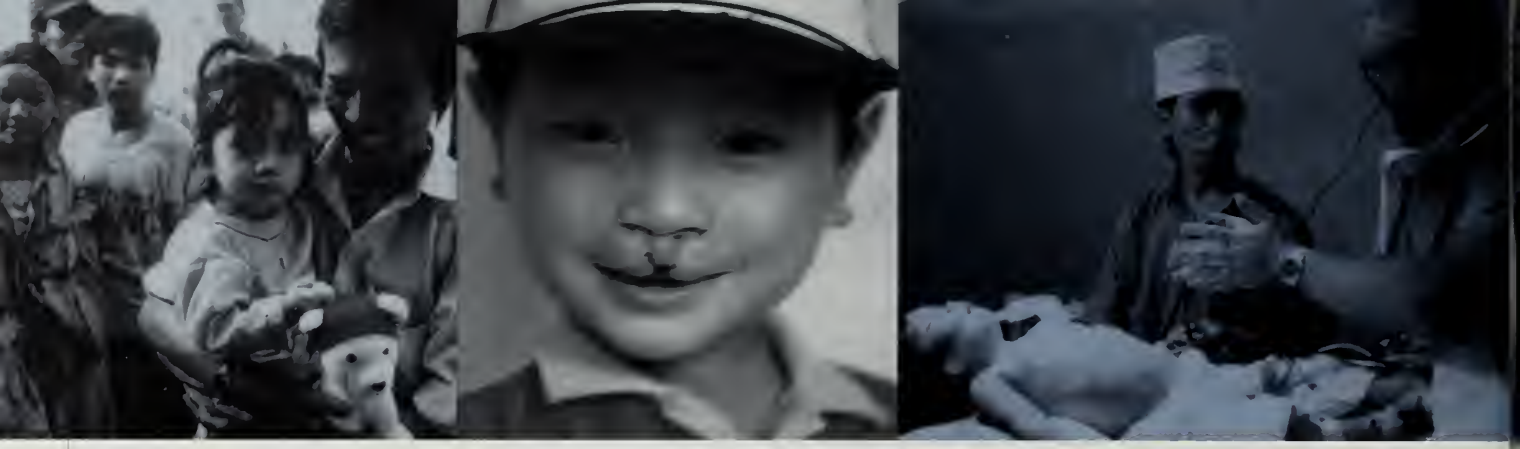
As the end of my tour of duty approached, all I wanted to do was make it home in one piece. I'd managed to survive for nearly a year and was determined to keep a low profile. "Short timer syndrome"—in which, with a month to go in his tour, a soldier would hunker down and refuse to take any risks—was a common phenomenon. This trend was reflected in a popular cartoon from the era that depicted a helmet on the ground with two boots sticking out from underneath it. When my last month came up, I permitted myself to think for the first time, almost euphorically, "I'm going to make it!"

And yet I'd already taken all kinds of foolish risks. I'd ventured with colleagues to the local beaches for cookouts, in spite of the constant danger of attack by the Vietcong. With a parachute strapped to my back, I'd flown at the controls of a military observation plane on one of its missions. In return for this privilege, I allowed the pilot to observe some of my surgeries in the OR; he was later killed when he accidentally smashed his plane into the side of a fog-shrouded mountain near Danang.

And on Sundays, I had frequently accompanied a young Vietnamese surgeon, Le Ba Dung, to visit attractions such as the old imperial tombs. On our way, I relied entirely on his intuition to judge if the road was safe.

Le Ba Dung had been assigned to work with me in the OR. When the war stopped at midday, as it customarily did because of the oppressive heat, he would often invite me to join him, his wife—an English teacher—and their children for lunch in their hut. We worked closely together for the entire year of my tour of duty. As it turned out, I never had a better friend in my life.

When it was time for me to leave Vietnam, Le Ba Dung and I promised to stay in touch. We corresponded until 1975, when the Communist North Viet-



SAVING FACE: Operation Smile's missian af surgically erasing the stigma of cleft lip and palate has transformed the future praspects af these Vietnamese children and many athers like them. Below, a woman in a Hanoi marketplace the authar visited.

namese took power, rendering communication impossible.

Into the Mouth of the Lion

When the MIA issue came to the fore in the 1990s, one of my colleagues in our plastic surgery practice mentioned that he was a friend of Bill Magee, the plastic surgeon who had co-founded Operation Smile. Magee had identified the need that many people in other countries had for cleft lip and palate surgery. This type of surgery seemed to provide an ideal focus because it can result in such dramatic improvements; a child goes into the operation disfigured and, moments later, emerges looking normal. Almost like magic, the child's future job and marriage prospects brighten considerably.

I joined Operation Smile on one of its earliest trips to Vietnam, in 1991. I figured that returning to Vietnam would be an opportunity to do good surgical work for people who really needed help—and I wondered if I might be able to track down my old friend, Le Ba Dung.

Flying back into Hanoi felt like placing my head into the mouth of a lion. I was returning to an area near where I had served my tour of duty, and I was afraid that the sight of rusty reminders such as old jeeps and military equipment would be unbearable.

But when I arrived, I was surprised to discover that most traces of the American military presence were gone. I later found out that, when the American military vehicles became useless thanks to a lack of spare parts, the Vietnamese had broken them down and sold the metal to the Japanese as scrap. The Japanese, in turn, had converted this material into passenger cars for export to American markets—an irony that delighted officials in Vietnam's postwar Communist regime, who rejoiced in turning a profit at their old enemy's expense.

Before our arrival, Operation Smile had sent personnel to alert the community. On our first day, more than a thousand people showed up to be screened. We knew that we had a finite amount of time, so triage was a necessary but wrenching part of the program.

Working from 7:00 a.m. to 10:00 p.m. for three solid weeks, we repaired about 300 cleft lips and palates. Some of the patients had gone to great lengths to seize the life-transforming opportunity. One ten-year-old girl had made the 30-mile bus trip alone, because her family couldn't afford to join her. Another patient was a man in his fifties. In a ten-minute repair job done with the use of a local anesthetic, I was able to erase the disfigurement that had burdened him with a lifetime of stigma, shame, and suffering.

As it had been during wartime, swimming provided a respite from all the hard work. When I announced one day, toward the end of the trip, that my colleagues and I were going swimming that afternoon, the Vietnamese director insisted, "But we have a very important meeting you and your team must come to!" In the end, all 35 team members grudgingly agreed to attend.

When we entered the meeting hall, we were astonished to see all 300 of the patients we had operated on, most of them still in bandages. At the front of the room was a barrel full of daffodils. One by one, each patient presented a daffodil to the doctor who had operated on him or her. You don't often see surgeons cry, but there wasn't a dry eye in the room.

I've since made several other trips with Operation Smile, two to Vietnam, three to Russia, one to Thailand, and one to the Philippines. On each, I've done mostly cleft lip and palate surgery, along with treating some burn patients. But I haven't done any more trips since the September 11 terrorist attacks increased the risks for Americans traveling abroad.

Chasing Shadows

On my first Operation Smile trip back to Vietnam, I'd asked after my old friend Le Ba Dung all over Quang Tri but no one would give me a clear answer. When I returned to the States from my second trip back to Vietnam in 1999—during which I had made another round of fruitless inquiries—I was stunned to find a letter from Le Ba Dung sitting on my desk. In it, he informed me that he had just immigrated to California. He'd recently been admitted to the hospital for a kidney stone, he explained, and while there, he had gotten hold of a physician directory and found my name.

To celebrate our reunion, Le Ba Dung's wife faithfully prepared all my favorite Vietnamese dishes, which she remembered from 25 years earlier. But conversation with my old friend was strangely limited and awkward. Sensing my confusion, one of Le Ba Dung's sons, now a grown man, pulled me aside to whisper, "My father's crazy now; they beat him up, you know."

Le Ba Dung, I learned, had been a POW in a communist re-education camp for five years. There the former surgeon attended ideology lectures in the morning and, a leather strap looped around his shoulders, pulled a plow through the rice paddies in the afternoon. He never worked as a surgeon again.

Le Ba Dung had emerged from the camp a broken man. Then, not long after he'd been set free, another conflict erupted between China and Vietnam, and he had been placed in detention for yet another year out of fear that he might subvert the war effort.

When the U.S. government established an amnesty program that allowed some of its former Vietnamese allies to immigrate to the United States, Le Ba Dung, his wife, and their four children to were able to relocate in 1999.

When I last saw Le Ba Dung, he was living in public assistance housing in Loma Linda, California. The former surgeon had found a job sewing buttons on shirts. Although he was not the same man whose friendship I had treasured in the past, we stayed in sporadic touch until 2002. But the last time I tried to contact him, his phone number had been disconnected, and no one had any forwarding information for him or his family. The disappearance of my friend remains a ghostly reminder of the elusiveness of closure for so many touched by the American experience in Vietnam. ■

Gerald Colman '66, an associate professor of surgery at Albany Medical College, has been practicing plastic surgery in Albany, New York, for 28 years.

WHEN WE ENTERED THE MEETING HALL, WE WERE ASTONISHED TO SEE ALL 300 OF THE PATIENTS WE HAD OPERATED ON, MOST OF THEM STILL IN BANDAGES.

An ophthalmologist reveals an eye for detail in the wild

VISIONS of NATURE

***photographs by* JAMES D. BRANDT**

WHEN I WAS EIGHT YEARS OLD, MY PARENTS GAVE me a 35-millimeter camera. It was my grandfather's beat-up camera from the 1930s, a Kodak Retina—some might say an early subliminal cue for me to become an ophthalmologist—and I was hooked. By the time I turned twelve, I had convinced my parents to let me turn one of our bathrooms into a darkroom.

I'd been interested in nature photography all along, but it became a serious calling during my sophomore year in college, when I joined a six-month expedition to Antarctica to do field research on antifreeze in fish. Although the experience fueled my desire to become a marine biologist, when I realized that jobs were scarce, I decided to go to medical school.

As a photographer, I'd always been interested in vision and optics, so ophthalmology seemed a natural choice for me. And now as an ophthalmologist with an eye behind the lens, I find myself drawn to the eyes of animals gazing back at me. I also find myself seeking patterns in nature, whether the nubby green ridges of a crocodile's back, the velvety feathers on an eagle's breast, or the tangled web of brown capillaries in a shark's watchful eye. ■

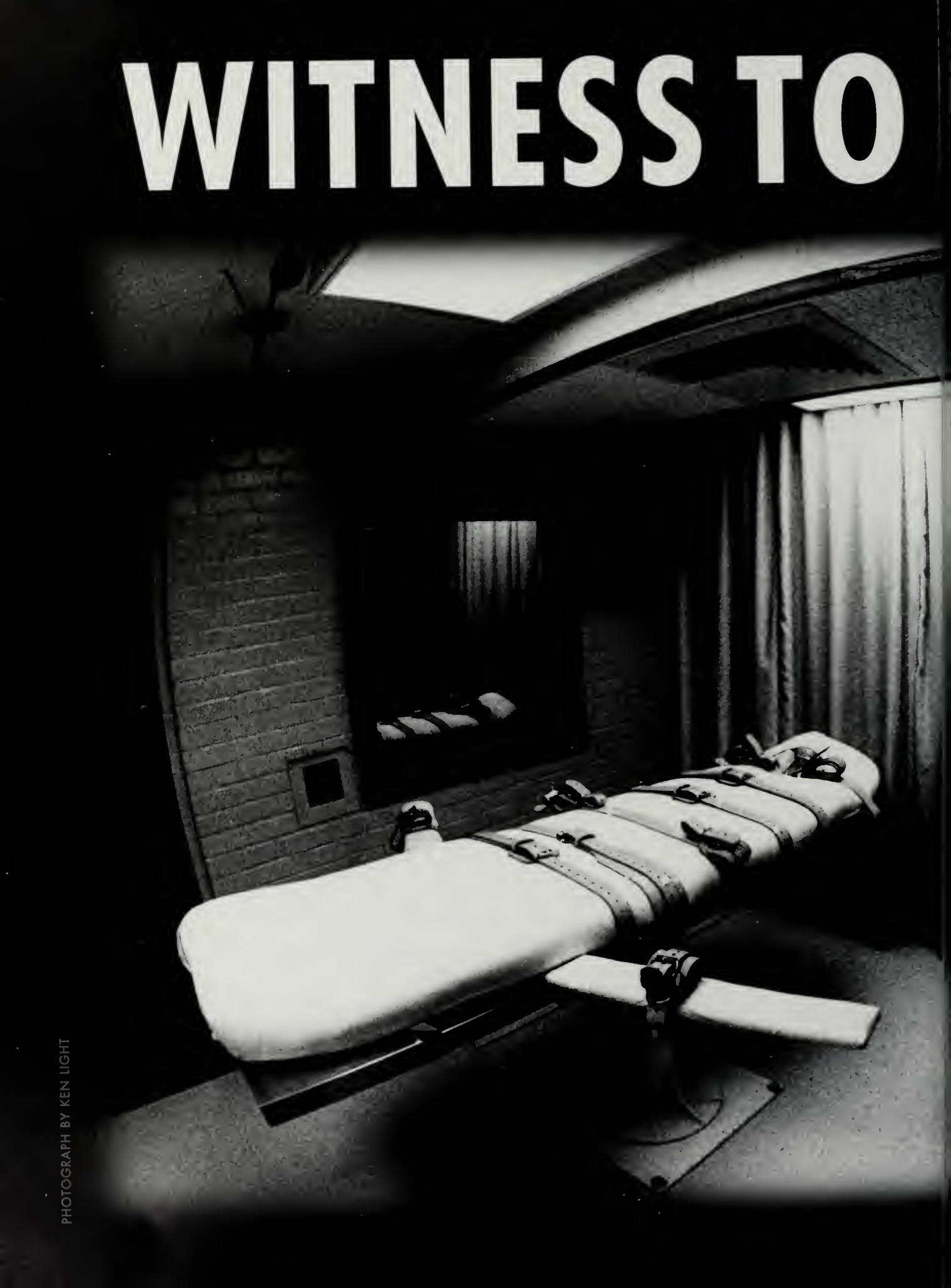
James D. Brandt '82 is director of the glaucoma service at the UC Davis Medical Center.

[Simple sea anemones, California's Monterey Bay]

[Clownfish, Great Barrier Reef, Australia, and Adélie penguin, Antarctica]

[Bald eagle, wildlife refuge in Florida, and emerald boa, aquarium in California]

WITNESS TO



PHOTOGRAPH BY KEN LIGHT

THE EXECUTION

Trained to preserve lives, a physician grapples with the execution of a friend on death row

by ANDREW G. DEAN

THE MORNING OF RON SPIVEY'S EXECUTION, MY WIFE AND I drove past an empty guard shack, down a half-mile of road, and past some duck ponds to reach the Diagnostic and Classification Prison in Jackson, home of Georgia's death row. We passed through two metal detectors and four steel-barred doors before walking down a long corridor to visit Ron for the last time. ▪ Five visitors had gathered with Ron in a wire-mesh–enclosed visitors' room. One hulking, black-clad tactical squad member

EVEN IN HIS CELL, HE HAD TO WATCH OUT FOR BOILING WATER HURLED HIS WAY AND RAZORBLADES ON STICKS.

was posted inside the room and another just outside the door. We joked and cried and swapped stories. Ron had blown his cash account on photo tickets, and we posed with him while another prisoner snapped away with a Polaroid. At three o'clock, the guards pronounced our visit over. Ron waved and smiled as he retreated down the hall, his six-foot-six, 340-pound frame flanked by a half dozen guards.

Ten months earlier, after more than two decades on death row, Ron had come within several hours of execution, but the Georgia Supreme Court had ordered a stay while deliberating whether death by electrocution constituted cruel and unusual punishment. After the court ruled in October 2001 that it did, lethal injection replaced the electric chair, and four chemical executions had quickly taken place in Georgia. Ron's was to be the fifth.

The State Board of Pardons and Paroles had listened, unmoved, to testimony about Ron's history of mental illness. One of my HMS classmates, Jay Jackman '64, had flown in from California to interview Ron and to file an expert declaration outlining Ron's mental problems. The Reverend Joseph Lowery, a legendary colleague of the Reverend Martin Luther King, Jr., had delivered an emotional appeal, declaring that the time to stop this kind of killing had come. It didn't matter that Ron was white, Lowery had told the board members; he was a human being, and the principle of nonviolence applied to all races—and to the state.

The pardons board had brushed aside evidence that Ron had tried to make amends while in prison, even saving several lives by reporting plots he had overheard to kill people on the outside. The other death-row inmates, in fact, considered Ron a snitch; once a gang of four attacked him using homemade knives and he nearly died from a penetrating chest wound. During one six-year period, Ron had refused to emerge from his cell, preferring solitary confinement to the dangers he faced outside its doors. Even in his cell, he had to watch out for boiling water hurled his way and razorblades mounted on sticks pushed through the bars.

Tangled Legacies

A few hours after our final visit with Ron, as we were returning to witness his execution, we saw an ambulance suddenly emerge from the prison compound and speed toward the freeway. We later heard that it had been transporting the widow of Billy Watson, the off-duty policeman Ron had shot to death in 1976. Mrs. Watson, who had conducted an impassioned, 25-year-long campaign to have Ron executed, was said to have collapsed an hour before the scheduled event. Officer Watson's son, himself a police officer, nurtured a different perspective. He had once told a reporter, "Hate is not in my vocabulary. I couldn't hate forever. I don't hate Spivey and I don't like the process."

Shortly before seven, the guards checked our identification and waved a metal detector over us before we climbed into a van reserved for Ron's friends and sympathizers. Following another security check at the prison entrance, we were led to the visiting area where we had said goodbye to Ron a few hours earlier. Posted on the wall were the familiar ground rules for visitors, detailing such instructions as how much skin female visitors could expose (not much) and the number of embraces allowed per session (one initial and one final). We could hear, but not see, invited members of the political and law enforcement communities and other witnesses for the state being escorted into a separate room.

During our vigil, I reflected on the stories that Ron had revealed to us during three years of monthly visits and frequent letters. His mother had barely attended school, he had told us, and she had taught herself to read food orders while working in a restaurant. When Ron turned 16, his parents had ordered him to quit school and go to work. His father made it clear that his birth had been an accident and that he remained unwanted. "He beat me like a dog," Ron recalled, "and he talked to me like one, too."

Ron ran away several times, and the authorities finally removed him from his home to rescue him from his father's abuse. While still a teenager, Ron took advantage of a deal to enter the Army rather than go to juvenile prison. After he was kicked out of the Army for bad behavior, he passed the high school equivalency test, but despite his high IQ, he never pursued additional schooling.

"In all my years in prison and out in society associating with other losers," he wrote us, "I found one thing that applied to 100 percent of us: none of us

had gotten a good education. I feel uncomfortable in a room full of well-educated people. So I sought out what I considered my own level of society. A lack of education forces you to live on the low end of all things."

In the winter of 1976, Ron's wife left him, taking their one-year-old daughter with her. "My world was in ruins," Ron told us. "I started drinking to numb the pain, and this led to losing a fine franchise business. I took tranquilizers, desperately trying to fight off the soul-numbing depression. Three days after the loneliest and most miserable Christmas of my life, I was taking tranquilizers and drinking all day. I had a confrontation with three men in a pool hall next to a bar in Macon, Georgia. I just snapped, and ended up killing one of the men." Ron then drove to Columbus, Georgia, where he tried to hold up a bar. He ended up shooting several people and killing one of them, Billy Watson.

"Because I had a gun when I went berserk that horrible night, a true American hero lost his life," Ron wrote us. "Officer Billy Watson, a 14-year police veteran, was moonlighting as a security guard at a nearby shopping center to earn extra money for his wife and children. During that night of madness I shot five total strangers, and two died. I caused great suffering that night. Since then, my guilt and horror have haunted me constantly. Nothing on earth—this prison, no one—can punish me like my own conscience has done."

Valley of the Shadows

Ron's expressions of remorse had not swayed his executioners, who were finally ready to deliver the ultimate punishment. Minutes before the ritual was to begin, we were ushered down a hallway lined with motivational posters, including one that featured a slightly cross-eyed, annoyed-looking eagle and the admonition to "Focus." Several vans were waiting outside, and we climbed into one that had heavy wire grillwork behind the driver. Guards locked the door from the outside as soon as we entered.

With us sat Ruth Enero, whom we had met several years earlier at a life-issues conference, where my wife, Consuelo, had been a speaker. Ruth had been flying from California to Georgia to visit Ron about once a year and keeping up a correspondence in between, but, as she had said, we could visit him more often without having to travel so far.

Throughout much of my life, I had maintained a vague interest in understanding what happens on death row, believing that outside authorities should monitor conditions there. But I had no direct experience with death-row inmates, and I had assumed capital punishment to be a routine part of the criminal justice system.

Later on, Amnesty International materials convinced me that execution is more expensive than life imprisonment, that there is no evidence that it lowers rates of violence, and that its application is enormously affected by the condemned person's race and his access—or lack of it—to competent legal representation. It had come as a surprise to me that the United States alone among Western industrialized nations still permits the death penalty.

My wife, by contrast, had a strong history of working in life issues and knew exactly where she stood; she had once belonged to a group that called itself People Against Everything—the death penalty, abortion, war, poverty, euthanasia, racism, and meat consumption. We're both physicians, though, which sets our baseline way over on the side of preserving life.

But it was our monthly visits with Ron that brought home the futility and waste of ending the life of a man who had sat on death row for more than two decades. Ron and I had nearly the same pre–World War II birthdate, and both of us were grandfathers. Although those who had never met him may have hated him, Consuelo and I found his conversation, sharpened by years of meditation (death-row inmates receive no occupational therapy because they are considered temporary), to be compelling and wise. We often found it difficult to reconcile the reality of the Ron we knew with the knowledge of those five hours of madness during which he had destroyed his life while ending the lives of two others.

As we sat waiting for the final leg of our grim procession to the death chamber to begin, we watched through the window grates as guards ushered people into the other vans. Seven o'clock, the time Ron was scheduled to die, came and went, but the vehicles remained motionless. We briefly hoped that the delay might mean that the authorities had issued a stay, but our hopes were extinguished when the vans began to crawl around the perimeter of the high prison wall, which was topped with coils of razor-sharp barbed wire. When we entered through a side gate, uniformed officers exchanged passenger lists, opened the hood of the van, scanned underneath with mirrors, and finally opened a second gate. Everyone involved in the ritual had a defined and compartmentalized role, which I realized helps to contain the emotion attached to executing a fellow human being.

Inside a long, low building, we were led to an audience space of perhaps 50 seats installed in graduated rows to afford a clear view of the proceedings. Through the three-part glass wall we could see Ron strapped to a surgical table. His arms were bound to armrests extending straight out to the sides, and the table was raised 60 degrees to a semi-vertical position. With a medical technician on the left and the warden standing motionless on the other side, the scene reminded me of the crosses at Calvary.

Ron could see us through the glass partition, and we tried to signal our support by raising our brows and widening our eyes, in violation of the strict printed instructions on execution decorum that we had signed. He met our eyes, letting us know that he appreciated our presence. Other spectators—mostly uniformed officers and prison guards—filed in to line the walls on either side of the viewing room.

The scrub-suited medical technician hovered near Ron, monitoring the intravenous stand, whose infusion line ran to Ron's right arm. A curtain hid

I WATCHED, KNOWING THAT HE WAS NOT IN PAIN, BUT WITH THAT HELPLESS FEELING OF HAVING JUST LOST A PATIENT.

the people who would be pushing the buttons to start the automatic injection of thiopental sodium, followed by pancuronium bromide, and finally potassium chloride.

The impeccably dressed warden stood ramrod straight as he asked Ron whether he had any last words. Ron pulled himself up on his surgical cross. "I've apologized to the warden and to the family of Mr. Watson," he said, "and I think they know, and I hope they believe, that if I had a million lifetimes, I could never say I'm sorry enough." After speaking of the failure of the death penalty to recognize the power of redemption, Ron ended with, "God has blessed me in a million ways with people who love me, people I love, wonderful people who do good things. I want all those that I love and that love me to leave this thing tonight without any ugliness, any hatred, any anger, any of that, and let Christ be first in their life."

"It's time," the warden said. "Would you like a prayer offered?" The prison chaplain uttered a few words, the warden signaled to the medical technician, and the chemicals began to flow. Ron started chanting something that sounded like, "Live and love!" from behind the glass, but the microphone had been turned off and we could hear only with difficulty. Then suddenly his eyes, still wide open, rolled back in his head, and he was silent. I watched with medical understanding, knowing that he was not in pain, but with that helpless feeling of having just lost a patient. For several minutes, Ron continued to breathe. His breaths then resolved into spasmodic gasps and his abdominal muscles began to twitch. Finally, his chest was completely still.

Two hapless disciples of Hippocrates, physicians from the Medical College of Georgia, appeared from the wings with stethoscopes. They listened to Ron's chest to ascertain the absence of the same heartbeat they had sought to sustain through his diabetes, obesity, and mental problems. Now they found it stopped, and the curtain was pulled.

An American Medical Association policy statement reads, "A physician, as a member of a profession dedicated to preserving life when there is hope of doing so, should not be a participant in a legally authorized execution." According to the newspapers, the dean of the Medical College of Georgia had sent a letter to the Department of Corrections withdrawing the school's support for even this ritualistic participation in executions, but within a few days, he was persuaded to continue.

States of Grace

We climbed into the van, which crawled back to the front gate where our car was parked. As soon as the van door opened, television crews trained bright lights on us and asked for our reactions. I said I was glad for Ron's sake that the electric chair was gone, but that I feared for the rest of us that lethal injection makes the process too easy. I did not mention that the scene I had just witnessed had evoked unsettling memories of our visit, several years earlier, to the museum of a death camp in Germany where chemical execution had been altogether too efficient.

Two months later, we had a reunion at the home of Pat Seaborn, one of Ron's cousins. She showed us the shrine in her family room, with Ron's ashes, the size 14 sneakers we had ordered for him, his glasses, and the brown scapular Consuelo had placed around his neck during our final visit. Although Ron was not Catholic, he had accepted this token, which is associated with dying in a state of grace, with religious feeling. He had kissed it after Consuelo's example, and the guards had allowed it to remain during his execution. We played the tape of his last words, which his daughter, Ronnie, hadn't heard, and she cried. Ron's granddaughter, who had seen him only once, played outside with a friend.

Pat told us that she and Ronnie had stayed at the main gate with the death penalty vigil group until it was time to leave. As they drove home, they saw clouds in the shape of a group of angels. As they watched, they thought they saw a shape come and join the other clouds, and then the whole host rose in the night sky. I kept thinking that we would see Ron again, perhaps somewhere on the road to Emmaus or the road to Jackson. The memories of warm conversations endure. ■

Andrew G. Dean '64 retired from the Centers for Disease Control and Prevention in 2002 and now teaches and consults in public health epidemiology.

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PELICAN BRIEF: While in Florida attending an ophthalmology meeting, James Brandt '82 photographed this brown pelican. The U.S. Postal Service recently turned the image into a commemorative stamp celebrating the centennial of the 1903 creation of Florida's Pelican Island National Wildlife Refuge, the first official wildlife refuge in the United States. More of Brandt's nature photography is featured in this issue.

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